SEPTEMBER, 1951

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

CONVENTION NUMBER

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Pages I-XX

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Sixteenth Annual Convention

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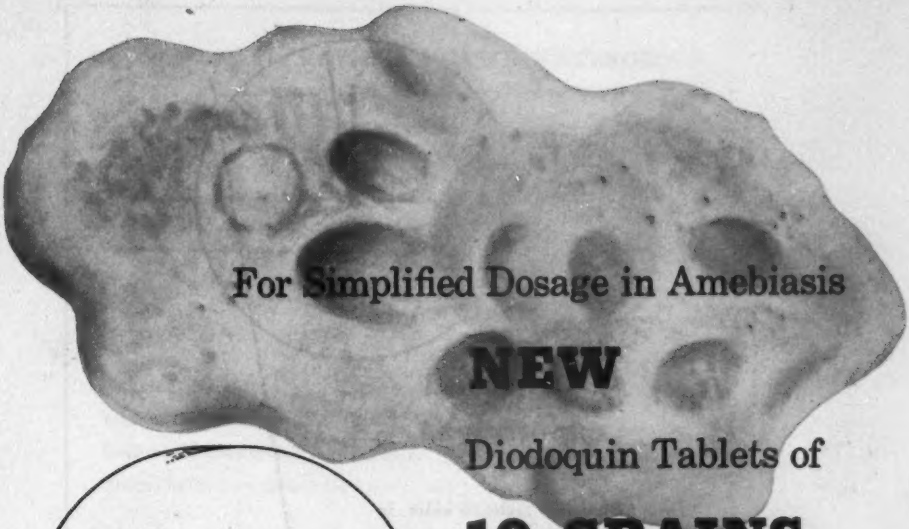

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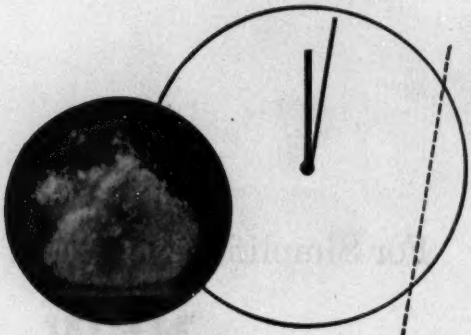

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(INCORPORATING THE AMERICAN JOURNAL OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

VOLUME 18 SEPTEMBER, 1951 NUMBER 9

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CONTENTS

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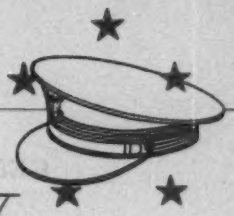

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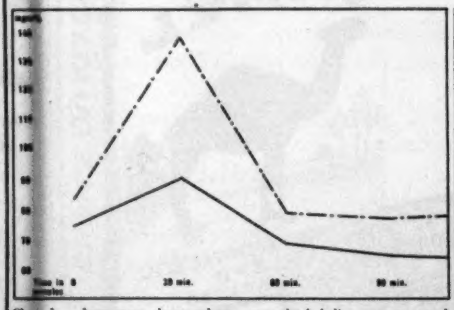

Chart 1 — Intravenous glucose tolerance test: dot-dash line, average normal curve of 30 patients; solid line, average of 55 patients with fatigue.

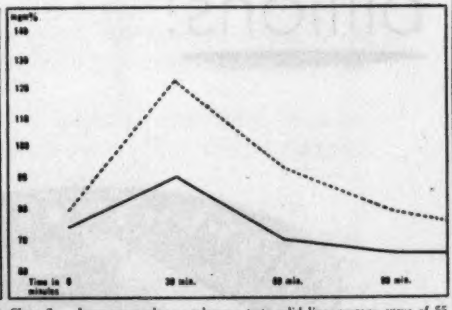

Chart 2 — Intravenous glucose tolerance test: solid line, average curve of 55 patients with fatigue; broken line, average curve of 15 of these patients given 1/50 grain of atropine sulfate hypodermically one-half hour before administration of glucose.

1. PORTIS, S.A., et al: J.A.M.A. 144:1162 (Dec. 2) 1950. 2. PORTIS, S.A.: J.A.M.A. 126:413 (Oct. 14) 1944.

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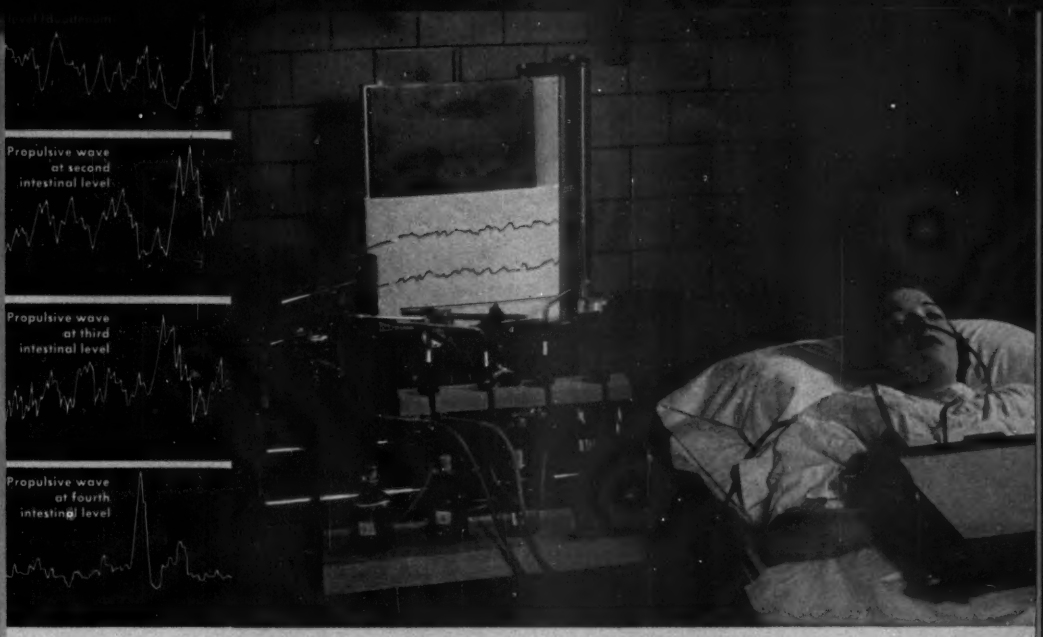

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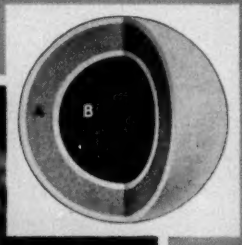

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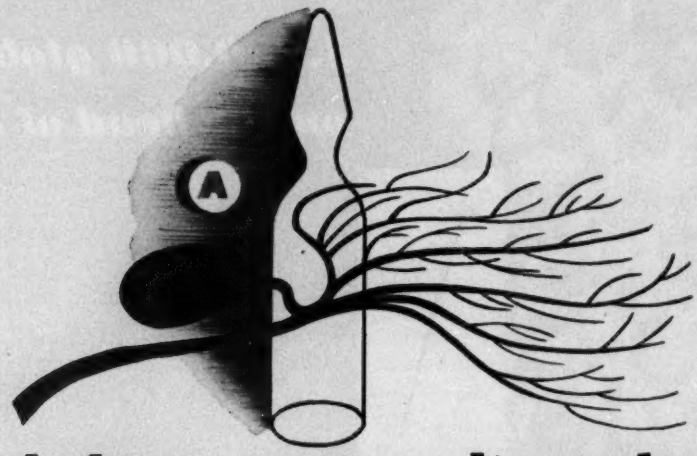

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A monthly journal of Gastroenterology, Proctology and Allied Subjects

Volume 18 SEPTEMBER, 1951 Number 9

SURGICAL DISEASES OF THE ESOPHAGUS*

RUDOLPH NISSEN, M.D.

New York, N. Y.

There is hardly a pathological condition of the esophagus which does not interfere mechanically with the food passage, thus posing, at one time or another, a surgical problem. Furthermore, organic obstructions of the esophagus, from whatever cause, present a mixed picture of mechanical and functional disturbances; in fact, some purely functional conditions demand surgical relief because of the failure of conservative treatment.

Of these functional conditions, cardiospasm is the most frequent and typical, although the name is somewhat misleading. There is no well-defined sphincter muscle in the gastric cardia area as there is at the pyloric end of the stomach. Probably the best explanation of the mechanism of cardiospasm is given by Hurst's description of what he calls achalasia, namely, that for some reason the physiological opening reflex of the cardiac end of the esophagus is lacking.

The cause of this reflex anomaly has been assumed by some to be of psychogenic origin; however, the correctness of this theory is still to be proven, and the results of psychotherapy in the treatment of cardiospasm are far from encouraging.

In the average case of cardiospasm antispasmodics are fairly effective. If obstructive symptoms become persistent with resultant progressive enlargement of the esophagus, mechanical treatment is indicated. Forceful dilatation by bougie is frequently highly satisfactory, but even in expert hands not free from danger. We witnessed several perforations, two of them fatal, in the preantibiotic era. The surgical procedure of choice is esophagogastrostomy which can be performed by transabdominal or by transpleural approach.

A combination of organic and spastic obstruction is present in the different types of diverticula. If located at the cervical part of the esophagus, neither diagnosis nor treatment pose any problems. Surgical removal, if done in a thorough way, is a safe procedure, and recurrences are exceptional.

The diverticulum of the middle part of the esophagus is assumed to be a traction diverticulum caused by shrinkage of inflamed lymph nodes. There is reason to question the validity of this theory. In two of our own cases which were operated upon because of their large size and severe clinical symptoms no lymph nodes were

*Presented before the Course in Postgraduate Gastroenterology of the National Gastroenterological Association, New York, N. Y., 12, 13, 14 October 1950.

encountered. We are inclined to believe that at least in some of them a pulsion mechanism may also be responsible. The symptoms are mainly those of widespread and severe esophagospasm. Excision of the diverticulum of the middle part of the esophagus involved a certain danger as long as no reliable method of closure of the esophageal incision was available. However, recent experiences with pedicled graft of lung tissue (upper segment of the lower lobe) tucked upon the suture line have dispelled these misgivings.

Surgery is imperative in the not infrequent complication, namely, perforation of the diverticulum into the bronchial tree.

This esophageal-bronchial fistula may manifest itself in the beginning by coughing spells and attacks of pneumonia. Esophagograms may fail to demonstrate the fistulous tract because of its minute diameter. The clinical picture therefore is more informative than x-ray examination. Bronchiectasis and lung abscess are bound to follow. Spontaneous closure does not take place. The operation can safely be performed by extrapleural paravertebral approach.

The diverticulum of the lower third of the thoracic esophagus is of the pulsion type, as is the cervical diverticulum. It may reach large proportions and it may be difficult to differentiate it from paraesophageal herniation of the stomach. Persistent symptoms of cardiospasm and the tendency to marked inflammatory changes of the sac and its surroundings call for surgery. Excision of the sac has the hazards and disadvantages mentioned in describing the traction diverticulum of the mid-esophagus. Excision or—in the absence of gastric hyperacidity—an anastomosis with the fundus of the stomach are the procedures of choice.

Benign tumors of the esophagus, if arising from the mucous or submucous layers, as papilloma or lipoma, lend themselves to endoscopic removal; however, two kinds of benign growth of the muscular wall are likely to require surgery if symptoms of semiobstruction become manifest; namely, the leiomyomata and the enterogenous cysts. While in both instances enucleation of the tumor is sufficient, intimate relations to submucous and mucous layers may cause accidental opening or even excision of mucosal areas, making resection of the esophagus unavoidable.

A rather dramatic situation may be created by severe hemorrhages due to esophageal varices so frequently present in portal hypertension. While portacaval or renal-splenic shunt operations are the most appropriate means of decompressing the varices of the lower esophagus, the severity and continuous character of the bleeding may call for local procedures. Endoscopic injections of the varicose veins with sclerosing solutions, or packing of the paraesophageal space under pressure are reported to be successful in one case but failing in the other. Resection of the lower esophagus and upper stomach is then the ultimate procedure, almost an act of desperation, if the more conservative procedures were unsuccessful.

Rupture of the esophagus may be induced artificially as an accident in esophagoscopy or probing and dilatation of an esophageal stenosis. It may also happen without external violence, as a so-called spontaneous rupture, probably caused by regurgitation and tissue digestion of hyperacid gastric juice. The resultant severe infection of the mediastinum is preceded by rapidly increasing mediastinal em-

physema, which, after a short time, makes itself palpable in the jugulary notch and the lateral parts of the neck. The esophagus rarely reaches the high degree of pressure as seen in bronchial rupture; therefore, decompressive measures are as a rule not too urgent.

The unavoidable infection of the mediastinum requires drainage. The prognosis of contamination of the mediastinum subsequent to rupture of the esophagus has decidedly changed since the introduction of antibiotics, fatal results having been practically eliminated.

The outlook for cases of congenital and posttraumatic stenosis of the esophagus greatly has improved, thanks to the recent advances in thoracic surgery. Atresia of the esophagus is usually located just above the level of the bifurcation. The distance between the lower and the upper esophageal segment, that is, the area of the atresia, may be longer or shorter. In most cases the lower segment is in communication with the trachea, thus giving a misleading x-ray picture of an air-filled stomach.

When, ten years ago, Cameron Haight was the first to succeed in an end-to-end anastomosis of the upper and lower segment immediately after birth, he opened a new field in esophageal surgery. There are, however, quite a few babies with atresia, in whom, due to poor general condition, too late a diagnosis and aspiration pneumonia, a less time-consuming operation would be preferable.

A palliative procedure in this sense should consist of the following steps:

1. External drainage of the upper esophageal portion in order to prevent aspiration of saliva accumulated in the blind sac.

2. Closure of the bronchial-esophageal fistula which can be done by a comparatively short transthoracic procedure.

3. Gastrostomy for feeding purposes.

4. Reestablishment of the foodway can then be done years later as an elective procedure by anastomosing the fundus to the upper esophagus pouch.

When the tremendous strides which thoracic surgery has made during the last twenty years are enumerated, the conquest of carcinoma of the esophagus occupies an outstanding place. While the technical methods which are successful today have been proposed long ago, the development of endotracheal anesthesia, the liberal use of blood transfusion, the maintenance of electrolyte balance, and the application of antibiotics have made the resection of the thoracic esophagus a fairly standardized and successful procedure.

It is understandable that the enthusiasm over technical achievements has induced us surgeons to lose sight of the final results. Today, in surveying ten years of radical surgery of carcinoma of the esophagus, we must admit that the end results are disappointing. They are even worse than in cases of carcinoma of the stomach.

Of course, as in carcinoma of the stomach, much depends on an early diagnosis, and it is probably timely to assert that overlooking of the initial phases of esophageal carcinoma is not so much the fault of the patient as of his doctor. There is the esophagogram, which, according to common opinion, is able to discover any kind of esophageal lesion. Unfortunately, this is not the case in the nonobstructing type. To be sure, the beginning of a malignancy is nonobstructive. You will probably argue

that there remains esophagoscopy, which should be able to discover small lesions of the mucosa, and help us by identifying their nature through biopsy. But, even in the hands of an expert esophagoscopist, minute pathological areas may be overlooked. Much more important, however, is the fact that the biopsy taken from the cortical part of a cancerous lesion may reveal only leukoplakia, as actually happened in three of our own cases.

This apparently benign finding compelled us to abandon the idea of surgery, only to be confronted two or three months later with an inoperable obstructing cancer. If we are aware of the fallacies of the esophagogram and of the difficulties of interpretation of a biopsy taken from the border of the lesion, we will find more cancers of the esophagus which are still amenable to radical excision.

Radical excision of a carcinoma of the esophagus, once it has spread into lymph nodes, is unrealistic, and from this angle we are probably correct in terming the operation in most of these patients a palliative resection.

The steps of the modern procedure may be briefly described as transpleural excision of the esophagus of any extent and bridging of the resulting defect by the stomach which is mobilized adequately from a transdiaphragmatic approach.

Discussion

Dr. I. Snapper:—This material is highly interesting. It should be stressed that a large diverticulum of the esophagus may give rise to an x-ray picture which seemingly indicates the presence of a mediastinal tumor. The large esophagus filled with food, often presents itself as a mass situated at the right side of the heart. Occasionally patients are suspected to have a mediastinal tumor although only dilatation of the esophagus due to cardiospasm is present.

Is operation indicated in a patient, in whom during examination for some other complaints, a diverticulum or leiomyoma of the esophagus has been demonstrated as an incidental finding? Personally, I think that if I had no complaints, I would not be operated upon for a diverticulum or a leiomyoma of the esophagus which had been found during an x-ray examination performed for other reasons. I would take a chance on the leiomyoma which grows slowly and usually becomes malignant only after many years,—but this conservative attitude is probably only due to the fact that I am a coward.

Dr. O. H. Wangensteen:—I have myself been a plumber of the alimentary tract for a good long while, longer than I like to admit; sometimes I have been down toward the lower end and sometimes toward the upper reaches; I have spent much time upon the cesspool of the lower ileum and colon, on bowel obstruction problems. A few years ago, somewhat inadvertently, I got interested in the problem of esophagitis and cardiospasm, and I have brought along a few slides which document a few increases of knowledge relating to the entities known as esophagitis and cardiospasm. I thought you might be interested in some of these observations.

The first is an x-ray film of Lyle Worden's stomach made in April 1936. On the first Sunday in September, 1939, he came into our University Hospitals because of massive hemorrhage from a bleeding duodenal ulcer. Because of persistent shock

despite several transfusions, an emergency gastric resection was done a few hours after admission.

When he recovered, I said to Mr. Worden, "Come back to the outpatient clinic and resume your dilations"—he had had about a hundred dilations of the esophagus during the preceding 5 years. Mr. Worden submitted reluctantly to two dilations but thereafter he didn't come for any more, and after a bit I sent for him and, much to my astonishment, he said he didn't need them. Years went by. The next film was made in April 1948 and the esophagus looks fairly normal. Moreover, he swallows anything, without any difficulty. There have been no more dilations. A number 46 French esophageal bougie goes down without trouble.

In 1942, a patient in his eighties, Carol Van Dyke by name, who had undergone gastrojejunostomy for an ulcer a few years previously came with a stomach ulcer and signs of esophagitis. A gastric resection was done for the ulcer. The symptoms of esophagitis promply disappeared.

To have seen this second occurrence of relief of esophagitis after gastric resection for ulcers made quite an impression upon me. And when Mrs. Ella Kuehn came along in 1944 with an esophageal stricture but no ulcer, the importance of what I had been privileged to observe in Lyle Worden and Carol Van Dyke began to have some meaning for me. There is a corkscrew-like stricture of her esophagus about 10 cm. above the cardia.

Mrs. Kuehn lived at International Falls, Minnesota, 40 miles from Minneapolis. She too had undergone, over a period of years, more than 100 esophageal dilations. She had great difficulty in swallowing. There was anasarca. Her plasma proteins were low. The internists believed she had gastric hemorrhage from portal hypertension and that the esophageal stricture was due to scarring of esophageal varices. She had a large liver, from polycystic disease. The internists proposed esophageal resection, for relief of the situation. I accepted her transfer to Surgery but said to Mrs. Kuehn, "I cannot resect your esophagus at that level without considerable risk." (It was 1944—a long time ago in esophageal surgery and her condition was poor.) I added: "I have two patients for whom I resected their stomachs, somewhat inadvertently—I grant you, but nevertheless, gastric resection cured their esophagitis. With your permission, I added, I would like to do the same for you." Whereas no one else in the University Hospitals went along with my idea, the patient did, and a three-quarter gastric resection was done. Two esophageal dilations were done during the next few months. Six years have gone by and Mrs. Kuehn has done very well, and there has been no need for further dilations. She swallows normally and can eat carrots, celery and hard rolls without difficulty. The plasma proteins are normal.

I want to present a couple more patients to give some of you a little more reassurance on the score of adequate proof, and we will come presently to the experimental evidence which, in the main, is the acid test.

In between these, I had a boy by the name of Clement Gagnon. He was about seventeen and since the age of one year had had trouble in swallowing. He was dilated many times, and when he was in the Outpatient Clinic one day after his

operation, Dr. William Focke of Poynette, Wisconsin, who was in the clinic with me one Tuesday morning in 1947 said to me, "I have a real test case and I will send him to you."

This was Harley Blackley, the most astounding case which has come to my notice. When I saw Harley Blackley in June 1947, he had carried a gastrostomy for eight years because he could not swallow his saliva. An x-ray picture of the esophagus could not be made until a No. 5 ureteral catheter was passed through the esophagus and drawn out of the stomach; following dilation we got a strictured picture. Moreover, the esophageal stricture was long. We dilated the esophagus up to No. 23 French and a gastric resection was done, eliminating the gastrostomy at the same time. For a period of a year, periodic dilation of Mr. Blackley's esophagus was carried out. More than 3 years have now gone by since operation and there has been no need for dilations for a long time.

So, I am inclined to believe that you can write it down as an established fact that, idiopathic stricture of the esophagus *is* acid-peptic stricture of the esophagus; and at this juncture I would like to show you some experimental work which indicates that spontaneous perforation of the esophagus is acid-peptic perforation of the esophagus.

Now, as you may well believe, one couldn't do this or make these observations without having his curiosity aroused. It should have been the other way around. We should have done the experimental work first, and then followed along with the gastric resection upon the patient but it is often this way. We make the observations, not knowing fully what they mean. Such is the great opportunity we have in medicine before us each day. We would do well to turn the eye of scrutiny upon entities we do not understand. Not every observation can however, be subjected to experimental scrutiny in a suitable test.

One of the first things I considered important to do was to establish whether or not perforation of the esophagus was a hydrostatic phenomenon; and, as you know, in bowel obstruction, perforation of the cecum is essentially a hydrostatic phenomenon. The cecum perforates first because its lumen is larger than the rest of the colon. In consequence, the stress upon its wall is greater. Perforation of the esophagus, as you will note from the slide is not a hydrostatic phenomenon. The normal esophagus of the dog resists, without rupture, more than an atmosphere of internal pressure, whereas, the fundus of the same dog's stomach will rupture at about 80 mm. Hg. pressure.

One of the next experiments performed was to tie off the pylorus of the dog giving him histamine in beeswax intramuscularly (30 mg. of histamine base daily); meanwhile, he was given fluids paraorally.

Much to our astonishment, of eight dogs treated in this manner 100 per cent developed a diffuse severe esophagitis within 4 days. In 4, or 50 per cent of the dogs, perforation of the esophagus occurred as well—all within four days. The stomachs of the dogs removed were perfectly normal.

John Hunter asked himself, "Why doesn't the stomach digest itself?" We are still asking ourselves that question, but bear that picture in mind.

Then, we dripped acid-peptic juice obtained from isolated canine gastric pouches, into the esophagi of other dogs, an outlet cannula being tied into the pyloric outlet so there was a sustained pressure of 20 c.c. of gastric juice within the lumen of both the esophagus and the stomach. The esophagus perforated readily, consistently while the stomach itself remained quite normal. Now, when tenth normal hydrochloric acid obtained from a bottle of the same pH employed in the above experiments, but containing no pepsin—when O.N/10 HCl alone was used, little or no effect upon the esophagus was noted.

We have heard much debate over the intervening years as to whether an ulcer is an acid ulcer or an acid-peptic ulcer. Nothing suggests more definitely the great importance of pepsin in the development of an ulcer than the experiment just cited. Such is the power of a catalyst! In fact, perforation of a cat's esophagus may occur as quickly as 20 minutes after the dripping of acid-peptic juice into the esophageal lumen is commenced. The esophageal mucosa contains very few mucus secreting glands. Moreover, the mucus in those glands is readily extruded and the capacity of the glands to make and extrude more mucus is readily exhausted. The ease with which perforation of the esophagus may be brought about because of the vulnerability of the squamous epithelium of the esophagus to injury by acid-peptic juice prompts me to suggest that spontaneous perforation of the esophagus is acid-peptic ulcer of the esophagus. Moreover, the instances of esophageal perforation reported by Harvey Cushing in the Balfour Lecture (Surg., Gynec. & Obst., **55**:1, 1932) were probably evidences of the great sensitivity of the esophagus to injury by acid-peptic juice regurgitated into the esophagus.

So much for esophagitis. I have no evidence of the same sort or as good for cardiospasm. I have some slides détailing a few observations and with your indulgence, I will show them, because I think they have some pertinence for the discussion.

With this background of interest you can see one might be led to believe that cardiospasm too is an acid-peptic-like disease, and I admit here—and confession is good for the soul—that I was foolish enough to believe that gastric resection might be a good operation for cardiospasm. I was mistaken in my first patient, because I, like a child, believed what was written on the diagnostic sheet.

For twenty-five years this lady, Miss Anna Lippman, had been carried on the records of the University Hospital as a case of cardiospasm. I shall come to the differential diagnostic point I want to make, presently, because I did not then recognize the difference, myself. She was cured not because she had cardiospasm, but because the diagnosis was wrong; she had esophagitis, so I was led to try gastric resection for cardiospasm for which it does nothing.

It gradually dawned on me what the nature of the difference was between esophagitis and cardiospasm. A patient with the latter condition, when surgery becomes necessary, has a dilated esophagus. In esophagitis on the contrary, the tone of the wall remains and it dilates very slightly, if at all. Megaesophagus is cardiospasm. The esophagus dilates because it has lost its tone. Auerbach's plexus is absent and the resultant situation is very much as in Hirschsprung's disease of the colon.

In the first patient submitted to resection of the esophagus, I excised the lower end, including the spastic terminal end, and the upper fourth of the stomach. He had scarcely left the hospital when he began to bleed. Some large tuberculous lymph nodes were found in the mediastinum at the time of operation. In consequence, I thought that he had a lighting up of an old tuberculosis. We sent him to a sanatorium for six months and he was no better. They sent him back to me, and meanwhile I had thought much about all this and initiated those experiments on the dog and cat (which should have been done much earlier) which taught me how susceptible the normal esophagus is to injury by acid-peptic juice; in fact, a little pedicled patch of gastric mucosa migrated up into the esophageal wall which caused an esophageal ulcer to appear opposite it. That patch of gastric mucosa in the esophagus will cause ulcer, even after a good portion of the rest of the stomach is excised.

The sensitivity experiments upon the esophagus indicated what I should now do with Norman Berg, my patient with cardiospasm who bled after operation. The remainder of the acid-secreting area of the stomach was excised and he has remained well.

I have now done five* additional patients with cardiospasm. The esophagus is mobilized intrapleurally with the employment of an extrapleural sternal splitting incision. The esophagus is mobilized and I resect as much of it as I can. It has been easy, in the presence of a dilated, tortuous esophagus to resect a fairly generous segment, 10 to 14 cms. usually. My colleague, Dr. T. Brannon Hubbard is studying the mobility of the esophagus by the balloon technic and another colleague, Dr. Fred Cross, has noted the uniform absence of Auerbach's plexus from the muscular coat of the esophageal wall in well developed cardiospasm.

So briefly, I would say that, idiopathic stricture of the esophagus is acid-peptic disease of the esophagus. Also that spontaneous perforation of the esophagus is acid-peptic ulcer of the esophagus. Cardiospasm is a different disease entirely, owing probably to congenital absence of Auerbach's plexus.

I do not share the enthusiasm of the English surgeons, Maingot and Ogilvie for the simpler Heller myotomy for cardiospasm. Grimson and others have reported hemorrhage after that procedure and that it should occur if the operation accomplishes what it sets out to do, is understandable, in the light of what I have said here concerning the sensitivity of the esophagus to injury by acid-peptic juice.

Question:—Recently, I think it is Palmer who uses x-ray therapy for reducing acid in the stomach. Do you think it has any effect in a moderate mild case, and so forth?

Dr. Wangensteen:—I don't know. I would be hesitant to use or advise x-rays to treat peptic ulcer. I will call on Professor Snapper.

Dr. Snapper:—I am not in favor of destroying the functioning mucous membrane of the stomach by x-ray. If the acid-producing part of the stomach has to be eliminated we had better ask Dr. Wangensteen to operate the patient.

*A total of 7 have been done.

STUDIES ON FACTORS INFLUENCING LIVER INJURY AND REPAIR*†

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The treatment of surgical lesions of the biliary tract is an ever present problem. During this past quarter of a century there has been a continuing decrease in the morbidity and mortality from such lesions. This can be attributed, in no small part, to an appreciation and application of the knowledge gained from animal experimentation designed specifically to answer problems in liver physiology.

In conditions of chronic liver injury we do not now have adequate methods of accurately quantitating moderate degrees of injury. The histological picture may show extensive damage while the laboratory tests indicate only a relatively minor damage. In contrast, acute hepatic cellular injury is almost universally associated with marked functional changes, even while the histologic evidences of parenchymal damage may be minimal.

The liver has an almost irresistible ability to regenerate after injury even under conditions that appear unfavorable. Likewise, it is also one of the most susceptible to damage from a variety of noxious situations.

The viability of hepatic parenchymal cells is markedly affected by anoxia developing under diverse situations. Not all anesthetic agents are hepatotoxic in themselves; yet during their use there may occur periods of oxygen starvation that can initiate processes leading to marked hepatic incompetency. In the normal liver short periods of anoxia may produce no irreparable damage, but in one whose functional reserves have already been reduced even short periods of oxygen starvation may be irreparable.

The observations of Shorr and his associates[1] and Frank and his associates[2] implicate the liver as the prepotent organ in the development of irreversible shock. The introduction of well oxygenated blood into the portal circulation affords amazing protection from the development of this serious situation. Massive or confluent centrilobular necrosis will occur in the livers of rats subjected to massive gastric distention[3]. This was more pronounced in animals previously subjected to partial hepatectomy, and the incidence increased with a prior depletion of the protein stores of the body. The importance of minimizing gastric or intestinal distention in patients with extensive liver injury has received little attention in surgical literature.

Dietaries adequate in composition and total calories facilitate the repair of an injured liver. It should be stressed equally that under-nutriture frequently condi-

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tions the extent of the hepatic injury which results after exposure to hepatotoxic agents. Goldschmidt, Ravdin and Vars[4] demonstrated that protein was the most important dietary constituent in conditioning the liver against injury by hepatotoxic agent. They demonstrated that elevated concentrations of hepatic lipids, prior to anesthetization, increased the incidence and severity of the injury. The inclusion of adequate amounts of protein in the diet for several days prior to anesthetization afforded some protection even in the face of elevated amounts of hepatic lipid. This general effect of adequate protein stores in facilitating the resistance of the liver against a wide variety of noxious agents has been amply confirmed by other investigators. As mentioned above, the state of protein nutrition also conditions the extent of injury developing from anoxia following gastric distention.

In man, the prothrombin concentration of the plasma may be markedly reduced following operations, during which conditions may arise leading to hepatic parenchymal injury.

It is quite difficult to assess the protein competency of many patients by the common laboratory tests. A carefully prepared clinical history and an accurate dietary record during hospitalization are often of more help than are extensive laboratory determinations. Using such criteria of protein nutriture the mean decline in prothrombin on the second postoperative day was 10.3 per cent in a well fed group, while the mean decline in a less well nourished group was 26.2 per cent.

Cholangiohepatitis is not so serious now with the increased availability of the newer antibiotics. Aureomycin has been used with gratifying results. While these agents do not relieve the underlying cause of the cholangiohepatitis, the control of infection allows operative relief under much more favorable circumstances. The striking results obtained by the use of antibiotics in preventing deaths following hepatic artery ligation[5,6] of the dog emphasizes in another manner the usefulness of antibiotic therapy.

There is increasing appreciation of the fact that the metabolic activity of the liver must be largely determined by the relative content of enzymes present within the cells. Experimentally many enzyme activities can be greatly attenuated by alterations in the protein status of the organ. This follows because enzymes are proteins. Dietary or metabolic situations that can increase or decrease the amount of its precursors should affect the concentration of enzyme proteins present. Rosenthal, Rogers, Vars and Fahl[7] have studied selected enzyme activities of regenerating rat livers from one half to eight days after a 70 per cent hepatectomy. With adenosine pyrophosphatase, rhodanese, choline esterase and common esterase, their activity per gram of liver protein started to decline just before the onset of mitotic activity and was reduced by approximately 20 per cent at the peak of mitotic activity and then gradually increased to normal levels. With arginase and alkaline phosphatase the inverse order of change was observed. The magnitude of the change was related to the postoperative changes in the animal's metabolism. Because of the significance of premitotic cytochemical changes it seems possible that stimuli to

cell multiplication may be transmitted through distortion of enzyme patterns as a result of environmental situations.

During liver repair diet can play a significant role in accelerating the process. From their early studies Goldschmidt, Vars and Ravdin[4] concluded that a diet rich in protein and carbohydrate but low in fat best facilitated the improvement of the patient before and after operation. Data were also obtained indicating that considerable amounts of fat could be included in the diet if sufficient quantities of high biological value protein were also fed. Under such a regime liver lipids decreased as rapidly as when the fat was restricted in the diet. Hoagland[8] has indicated that dietary fat need not be so severely restricted, as was earlier suggested, in the treatment of patients with infectious hepatitis. Besides making the meals more palatable the caloric needs of the patient could be more easily supplied.

Vars and Gurd[9] have clarified further the role of dietary protein in affecting the growth of regenerating liver. After partial hepatectomy in the rat, new liver protein is formed in a definite relationship to the quality and amount of protein fed in a calorically sufficient diet. When calories were restricted below basal needs liver regeneration bore a definite relationship to the nitrogen balance. Proteins lacking in essential amino acids may lead to no greater liver regeneration than if no protein was fed.

Rogers, Ferguson, Friedgood and Vars[10] have investigated liver regeneration during the feeding of high fat diets. Isonitrogenous and isocaloric diets containing up to 50 per cent of the total calories as fat did not impair the restoration of liver protein.

It has been of importance to determine the ability of the liver to regenerate after common duct occlusion, for it is well accepted that degeneration and repair can occur simultaneously in infectious hepatitis and homologous serum jaundice. This problem has been investigated by Ferguson, Rogers and Vars[11], who have observed the regeneration of the partially hepatectomized rat's liver in the presence of common duct occlusion produced either before or after lobectomy. When placed on an adequate dietary the liver will regenerate, as evidenced by an increase in mitoses and number of cells and an increase in hepatic parenchymal protein.

These conditions are not an exact duplicate of those in man presenting a common duct stricture or stone in that there was no cholangiohepatitis present. However, we have now obtained evidence in man that regeneration can take place in conditions of recurrent cholangiohepatitis. This has been observed by the presence of mitotic figures in liver specimens, obtained at the time of operation after what we believe to be optimum and adequate preoperative dietary therapy.

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Discussion

Dr. I. Snapper:—I can heartily agree that many of our patients are killed by administration of too large doses of barbiturates. This holds true for several of our asthma patients and also for a certain number of surgical patients.

There are many countries in the world where surgical patients who need injections of morphine derivatives receive at the same time metrazol and cardiazol. In this way the depressive action of morphine on the respiratory center is neutralized but the analgesic action remains intact. It is wise to combine the administration of morphine to postoperative patients always with metrazol or coramine, just as Dr. Vars demonstrated today.

Concerning the influence of diets on liver degeneration in general, on postoperative liver degeneration in particular, the following observations may have some importance. In the Orient, where the protein ingestion of the population is minimal, and where healthy people have usually less than three grams of albumin per 100 c.c. of serum, hepatic necrosis, or acute yellow liver atrophy is decidedly uncommon. In these areas where due to the low protein intake liver cirrhosis is extremely frequent, hepatitis, whether viral or infectious, is a rather innocuous disease.

I have seen hundreds of cases of jaundice in Chinese patients, but only one case of hepatic necrosis in a pregnant woman. In the same area I have encountered several cases of hepatic necrosis in white people. So far as clinical experience goes it seems that in the human, low protein diets per se do not favor the development of hepatic necrosis during hepatitis, or after anesthesia, though they lead to Laennec's cirrhosis.

These Oriental diets are not only low in calories, and low in protein, but also exceedingly low in fat, especially in animal fats and cholesterol. In view of the conclusions of Dr. Vars maybe one should stress more the low fat than the high protein content of the diet in the treatment of human liver degeneration.

It is dangerous to use results of liver studies obtained in rats and dogs for the explanation of the causation of diseases of the human liver. The rat has no gallbladder and the function of the rat's liver is completely different from the human liver. After the administration of bicarbonate of soda the rat produces large quantities of hydroxybutyric acid. This does not happen in the human! The liver of the dog cannot synthesize hippuric acid which is produced in large quantities in the human liver. Acetone appears in the urine of the dog, as soon as all the glycogen of the liver has disappeared, but this doesn't hold true for the diabetic patient. The livers of the diabetics who die in severe ketosis contain lots of glycogen. Thus one has to be careful in using the results of the experiments on the liver function in rats and dogs for the explanation of human liver disease.

Dr. O. H. Wangensteen:—I should like to speak from the standpoint of a surgeon. My point of view is a little different and the approach to the problem is different.

Speaking for surgeons generally, I would say that the work of Dr. Ravdin and Dr. Vars and their associates at Philadelphia, has been a source of great satisfaction to surgeons. I am certain that surgeons generally have implemented some of the preoperative methods which these men have observed beneficial in animals.

I think Dr. Snapper did us an important service when he pointed out certain distinct differences between the behavior of the liver of man and animals. I would point out in particular, with reference to the dog, though Dr. Vars spoke largely of the rat, that a dog has a different liver even bacteriologically.

Surgeons used to debate for long years after Frank Mann, in the middle '20's, said if you dropped a bit of liver about the size of the distal phalanx of the thumb, into the peritoneal cavity of a dog, it would kill the dog. Dr. Dragstedt did a little novel thinking on this and came up with a brilliant idea. He, too, like others confirmed Mann's observation over the toxicity of implanted liver tissue in the dog when, however, Dragstedt dropped liver tissue from new born puppies into the abdomen of other dogs, nothing happened. Dragstedt thereby resolved, for once and all, the whole question of what the nature of so-called toxicity of the dog liver was. It is probably not out of place to point out here that Wohlbach had described anerobic organisms in the dogs' liver much earlier. Markowitz reported recently that dogs survived ligature of the hepatic artery when penicillin was administered simultaneously. However, he probably ligated the hepatic artery proximal to the gastroduodenal artery. As Dr. Lewis, one of my associates, has shown, the human liver is not as toxic as the dog's liver, probably because arterioles are not present.

I want to say one other thing about the surgeon and the liver. I would not agree with one of the essayists that metastases in the liver constitute a contraindication to operation. I want to mention now only the sensitivity of the liver to anoxia. I suspect that goes for every liver; the dog as well as the human liver.

The first time I took out the right lobe of the liver in man, I had a clamp on the vascular afferent inflow for 33 minutes and nothing happened. When I excised in a second patient, the left and about two-fifths of the right lobe of the liver, occluding the afferent vascular inflow for 24 minutes, the patient became oliguric and somewhat confused. However, he got well. I then did a third man in which the afferent inflow was arrested for 10 minutes during excision of the left lobe. For 20 minutes the blood was allowed to flow through the liver again before we removed several metastases from the right lobe; and the second interval of arrest of hepatic vascular inflow was 15 minutes. This patient was an alcoholic and quite obese. He had no drop in blood pressure during the operation, a few hours later, however, he became hypotensive and never fully recovered, and within twenty hours he was dead.

At my suggestion, my colleague Dr. Raffucci began detecting the problem in the experimental laboratory. We were astonished to learn how sensitive the dog's liver is to anoxia. In fact, in consequence of those studies, we do not occlude the vascular inflow to the liver for more than a minute at a time.

LIVER BIOPSY*

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I clearly recall standing on this very platform four years ago while partaking in a Symposium on Liver Disease in which all participants were armed with clinical data based upon their experience with hundreds of cases of hepatitis, thousands of serial liver function tests but with few liver biopsies with which to back their opinions. At the time we thought we knew the liver fairly well. Since then, however, with the advent of liver biopsy as an almost standard diagnostic procedure, we must conclude that our knowledge of the subject of diseases of the liver is still in the preliminary stage.

The diagnosis of liver disease by means other than biopsy is often difficult. While clinical findings and liver function tests may indicate the presence of liver damage, it often remains for the liver biopsy to provide a conclusive diagnosis.

Fortunately, needle biopsy of the liver is a relatively simple and safe procedure which can be done at the bedside and requires no elaborate operating-room set-up. Although a biopsy of the liver may be taken by means of the peritoneoscope which also permits visual inspection of the liver, the method most generally employed is that of direct needle biopsy through the anterior abdominal wall or through the thorax. Various types of needles have been described but I have found the Vim-Silverman needle most satisfactory.

While the abdominal approach is employed in cases where the liver extends four or more fingers below the costal border, the thoracic approach has the advantage of permitting biopsy in a liver of normal size. The latter method can be used only in a cooperative patient who can maintain a period of apnea of 10 or more seconds. It should not be employed if there is a history of recent disease of the right pleural cavity or lung.

Certain precautions must be observed regardless of the mode of approach:

1. The patient should be typed and cross-matched and blood should be available for use if needed.

2. The prothrombin time should be at least 70 per cent of normal and the bleeding and clotting time should be normal.

3. Ascitic fluid, if present, should be evacuated prior to biopsy.

Where a focal disease such as carcinoma is suspected, specimens are obtained by both abdominal and transthoracic methods to increase the chances of a successful "strike".

The chief source of danger is hemorrhage and hence biopsy is best omitted in the presence of passive congestion of the liver even with normal prothrombin, bleeding and clotting time. Nearly all of the reported deaths from liver biopsy have occurred following hemorrhage where the thoracic approach was employed. This probably has been due to the fact that the needle had become fixed between two

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ribs and respiratory motion resulted in a tear of liver substance. Bile peritonitis with fatal outcome has been a rare complication caused by the needle entering an obstructed and dilated biliary duct.

Technic

The technic of liver biopsy by anterior abdominal approach has been frequently described and requires no elaboration here. Careful attention to detail is an important prerequisite for successful biopsy by the transthoracic method. No sedation is required. The patient is brought to the right edge of the bed and tilted slightly to the right by means of a pillow placed beneath the left thorax. The upper margin of the liver is percussed during deep expiration and a nick in the skin is made with the finger-nail in the right costal interspace in the mid-axillary line. This interspace is usually the ninth but may be as high as the seventh. The patient is given breathing exercises until he is sure that he understands the procedure and to

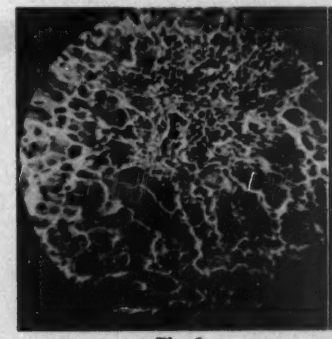

Fig. 1

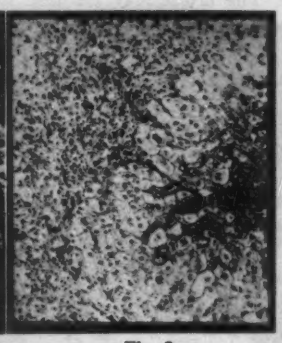

Fig. 2

Fig. 1—Acute viral hepatitis. Note the marked periportal round cell infiltration. There is no distortion of liver cords in this section.

Fig. 2—Chronic active viral hepatitis six months after the onset. Note the intense periportal infiltration at the right, large vacuolated cells containing two nuclei in the center of the field, with distortion of the lobular structure and early fibrosis at the left.

determine how long he can hold his breath in deep expiration. An apneic period of 10 seconds is a minimum requirement.

The skin over the area selected in the appropriate intercostal space is infiltrated with 2 per cent procaine and an incision is made with a scalpel, following which the intercostal muscles and the parietal pleura are anesthetized. The diaphragm and Glisson's capsule are infiltrated through a 3 inch, 22 gauge needle with the patient maintaining deep expiration. The needle should be pointed toward the xyphoid process. The patient is rested for a short period and the Vim-Silverman needle is then introduced with the inner cutting needle retracted just out of view. The outer needle is pushed into the liver for 1 cm. and the inner needle pushed forward to its hilt. The inner needle is held firmly and the outer needle advanced 2 cms. to help detach the liver fragment from its lateral attachments. Finally both needles are rotated together 90 degrees and are withdrawn. The entire procedure

is done with the patient holding his breath in expiration and requires 12-15 seconds. A collodion dressing is applied to the site of entry and the patient is kept in bed under strict observation for 24 hours.

Aftereffects

At the time of biopsy most patients experience a dull pain in the region of the epigastrium which is usually transient. There is usually tenderness at the biopsy site for 24-36 hours and occasionally this may be severe. A perihepatic friction rub may be heard in some cases. If chest x-rays are taken routinely in all cases biopsied, a mild pneumothorax may be noted in a considerable proportion of patients but spontaneous resorption of air is the rule.

Rarely, liver biopsy is followed by a febrile reaction which may persist for several days. In my experience this complication has always responded favorably to penicillin. The latter may be used prophylactically before biopsy.

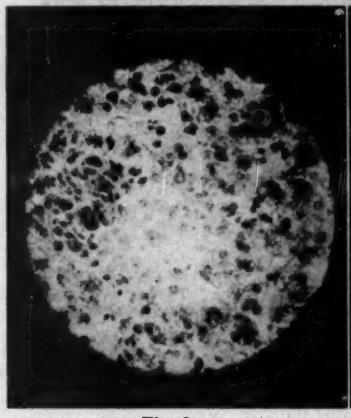

Fig. 3

Fig. 4

Fig. 3—Obstructive jaundice due to common duct stone. Note the polymorphonuclear leucocytic exudate.

Fig. 4—Obstructive jaundice. Hepatic lobules are unaltered but bile channels are distended.

Value of Liver Biopsy

1. Systemic diseases.
2. Differentiation between intra- and extrahepatic jaundice.
3. Focal hepatic diseases.
4. Diffuse hepatic diseases.

1. *Systemic diseases:*—In certain systemic diseases the liver provides a readily available and frequently the only source of biopsy material for pathologic study. Thus it is useful in acute miliary tuberculosis or brucellosis where no other biopsy material is available. Klatskin[1] has found this diagnostic method extremely valuable in the diagnosis of Boeck's sarcoid where tubercles may be found in over 70 per cent of cases by liver biopsy. Similarly, in hemochromatosis where skin biopsy may

not demonstrate the presence of hemosiderin, liver biopsy is almost invariably heavily laden with this iron deposit.

2. *Differentiation between intra- and extrahepatic jaundice:*—Needle biopsy has provided an important contribution to clinical diagnosis in the differentiation between hepatocellular and extrahepatic jaundice. In viral hepatitis there is a fairly consistent cytologic pattern which varies with the duration of the disease. The primary features are the presence of a severe round cell infiltration in the portal zones (Fig. 1) and focal intralobular necrosis of individual cells. Thus the portal area is enlarged and the exudate is primarily lymphocytic, although some monocytes and eosinophiles may be present. There is a lobular deformity and a derangement of the normal pattern of the hepatic cords. The liver cells are swollen while the nuclei appear enlarged and more than one may be present in a single cell (Fig. 2). These cellular changes are pathognomonic of hepatitis. Despite the appearance of

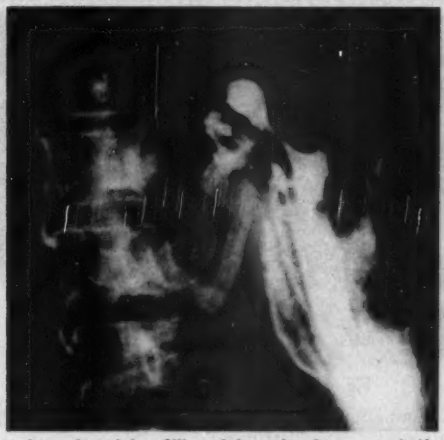

Fig. 5—Small hiatus hernia and nodular filling defects in the upper half of the stomach due to extrinsic masses in the liver. Gastroscopy revealed a normal mucosa.

vacuolization, there is an absence of stainable fat. In severe forms of hepatitis occasional bile duct budding may be encountered, but there is no dilatation of bile ducts and an absence of bile plugs. Central necrosis is usually present.

In extrahepatic biliary obstruction, bile stasis is the predominant feature. Both intra- and intercellular canaliculi contain bile plugs and the biliary channels are distended. Exudate may be present in the portal areas but polymorphs rather than lymphocytes predominate (Figs. 3 and 4). Doctor Vars spoke of the presence of multinucleated cells in the experimental forms of extrahepatic jaundice in animals. This is unusual in obstructive jaundice in the human, the presence of multinucleated cells favoring the diagnosis of hepatitis. In extrahepatic obstruction of long standing there is active periportal fibrosis but this is always extralobular and the nodulation, which is characteristic of the common forms of cirrhosis, does not occur.

Biopsy diagnosis is more accurate than combined liver function studies in the various forms of jaundice. However, it is important to stress that sound clinical

judgment must not be discarded in favor of a single laboratory study, even a liver biopsy. While it is usually early in the course of an obstructive jaundice that the morphologic changes may resemble virus hepatitis, operation should not be deferred where the history and clinical findings strongly suggest an extrahepatic factor.

3. *Focal hepatic disease:*—Liver biopsy is useful in confirming a clinical diagnosis of hepatic carcinoma and occasionally will uncover such disease which was unsuspected. This is illustrated by the following case:

M. F., female, age 42, with a past negative history, was referred for investigation of "explosive bowel movements" which started following a heavy Christmas dinner and persisted for four weeks. There had been no weight loss and she felt well apart from the sudden change of bowel habit. Physical examination was negative. The liver edge was just palpable but this was not considered significant at her

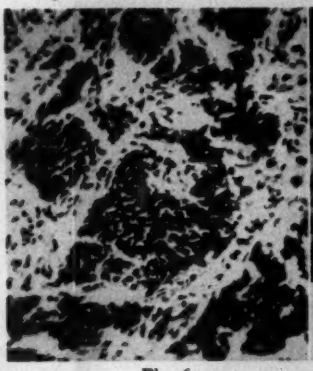

Fig. 6

Fig. 7

Fig. 6—Needle biopsy showing infiltration of liver by intensely stained cells suggesting squamous epithelial origin (possibly oat-cell carcinoma).

Fig. 7—Metastatic adenocarcinoma of the liver; the primary source was not discovered. X-rays of the gastrointestinal tract and gallbladder were normal.

initial examination. Sigmoidoscopy and barium enema were normal and the stools contained no occult blood; blood count and urinalysis were normal. During the course of a small intestinal series, several nodular defects were seen in the upper half of the body of the stomach as well as a small hiatus hernia (Fig. 5). Gastric analysis and gastroscopy were normal. Liver function studies revealed a normal serum bilirubin, thymol turbidity, cephalin flocculation and alkaline phosphatase, but there was a 12 per cent retention of bromsulfalein after 45 minutes. As the diagnosis was obscure, and it was believed that the above noted defects might be due to extrinsic pressure from nodules in the liver, a needle biopsy was done. Sections showed a metastatic carcinoma, the primary source probably arising in squamous epithelium (Fig. 6). A chest x-ray and esophagogram were normal, hence the origin of the lesion was never discovered. During the following month the liver became tremendously enlarged until it filled almost the entire abdomen. Jaundice

made its appearance and she died from a sudden massive hematemesis ten weeks after the onset of her initial symptoms.

Since both primary and metastatic carcinoma of the liver are focal diseases, the accuracy of liver biopsy is variable and naturally depends upon the extent of liver involvement. The presence of carcinomatous tissue on needle biopsy usually indicates extensive involvement and precludes the advisability of surgical procedures other than palliative (Fig. 7). A negative biopsy must not be considered conclusive. As indicated above, when carcinoma or any other focal disease is suspected, biopsy material should be obtained by both the thoracic and abdominal approaches if possible.

4. *Diffuse hepatic diseases:*—In the great majority of cases, the diagnosis of acute viral hepatitis can be arrived at without liver biopsy, by correlating the history and physical findings with liver function studies. In some cases of acute hepatitis

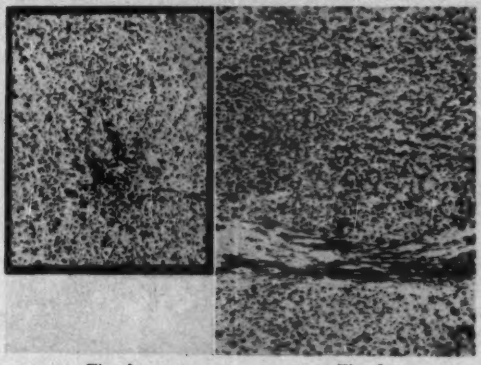

Fig. 8 Fig. 9

Fig. 8—Periportal round cell infiltration with normal lobular structure. Patient had viral hepatitis 1 year prior to biopsy and was asymptomatic with normal liver function studies.

Fig. 9—Nodular hyperplasia following severe hepatitis. The lobular structure is replaced by tightly packed cells enclosed in dense fibrous bands devoid of liver cells. This is the usual type of cirrhosis (toxic) resulting from virus hepatitis.

without jaundice, however, abdominal pain associated with marked right upper quadrant tenderness and without hepatomegaly may simulate acute cholecystitis. Cholecystograms taken during the acute phase of hepatitis without jaundice may be normal, show poor gallbladder visualization or, as occurred in two of my patients recently, demonstrate calculi which proved unrelated to the symptomatology. The cytologic changes in such cases are similar to those described above in hepatitis with jaundice.

The relationship between infectious hepatitis and cirrhosis has become the subject of considerable discussion at present. In this regard needle biopsy of the liver has been most helpful. The question of whether Laennec's cirrhosis may develop as a result of infectious hepatitis is still disputed. Several years ago Klatskin and I[2] published our findings regarding the sequelae based upon our observations in over 300 cases of chronic hepatitis. It was our belief that in the great

majority of cases clinical recovery followed ultimately. Biopsy specimens, however, taken many months after apparent symptomatic, physical and laboratory restitution to normal may show periportal round cell infiltration but without fibrosis (Fig. 8). In other cases, jaundice persisted for months and liver function studies gave results suggesting extrahepatic obstruction. This form of the disease has been termed "cholangiolitic hepatitis", and liver biopsy even after months of jaundice showed little distortion of normal liver architecture. These patients frequently looked and felt well apart from the presence of deep icterus.

In others in whom the initial disease or subsequent relapse had been severe, however, a condition of nodular hyperplasia developed. The liver was frequently

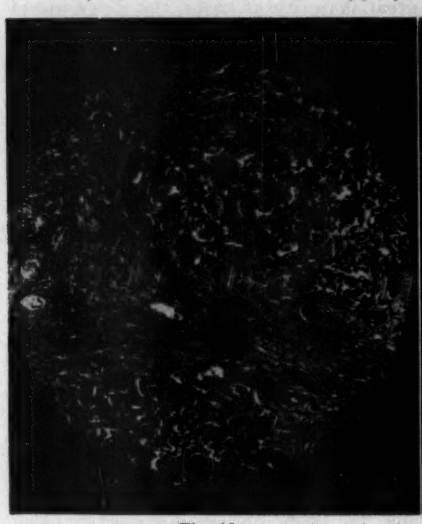

Fig. 10

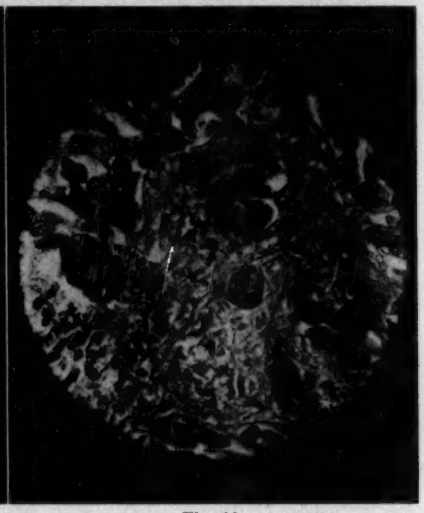

Fig. 11

Fig. 10—Laennec's cirrhosis in 38-year old man. Biopsy taken 3 years after severe homologous serum jaundice. Note the intralobular fibrosis and distortion of normal lobular structure. This form of cirrhosis is a rare sequel of viral hepatitis.

Fig. 11—Laennec's cirrhosis following severe homologous jaundice. Note the round cell exudate, fibrosis and multinucleated cells.

markedly enlarged and presented nodularity which, when localized to the left lobe, protruded visibly and suggested a tumor mass. On biopsy the liver cells are noted to be closely packed and arranged in no orderly lobular fashion (Fig. 9). Fibrous tissue is present in dense bands completely devoid of liver cells, representing compressed reticulum. This is in sharp contrast to the regular pattern of bands of fibrous tissue intertwined among small areas of liver cells usually seen in Laennec's cirrhosis. At the time we reported these observations, we were handicapped by scanty biopsy material. Watson and Hofbauer[3] subsequently presented cases of cholangiolitic hepatitis which eventuated into the pathological picture of Laennec's cirrhosis, and the current use of needle biopsy in cases of hepatitis has shown that while the

characteristic lesion is that of nodular hyperplasia, occasionally the pattern of Laennec's cirrhosis appears (Figs. 10 and 11).

I have often been asked the question, "What difference does it make to the patient whether his cirrhosis is coarsely nodular or of the Laennec variety?" While it is true that regardless of the type of cirrhosis the prognosis is guarded, under modern therapy stressing nutritional aspects the prognosis of Laennec's cirrhosis is not a hopeless one since usually some improvement under therapy may be anticipated. In coarse nodular cirrhosis, on the other hand, the disease appears to inexorably progress to an ultimately fatal course regardless of method of treatment.

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Discussion

Dr. I. Snapper:—We must accept that liver biopsy will have at least a 1 per cent death rate, but this does not mean that out of the first hundred patients one should die. Because of the statistical error one may do 200 or 300 punctures before a fatality is encountered! Though it is not a very dangerous procedure, certain precautions are necessary. For example it is wise not to do a liver puncture in patients with congestion of the liver due to right heart valve failure, because there especially the danger of hemorrhage exists.

Liver puncture is certainly a useful procedure and the best results are obtained in the differential diagnosis of jaundice. Nevertheless, I doubt whether such biopsy is necessary in all cases of jaundice. Personally I like to avoid this procedure in jaundiced patients when a satisfactory diagnosis can be reached by clinical observation and by different liver function tests.

In my hands the results of the liver puncture for the diagnosis of carcinoma of the liver have not been too favorable. I have encountered many patients with liver carcinoma where I miraculously punctured exactly between the different tumor masses. Lately we saw a patient with liver cirrhosis where we had good reason to suspect that a hepatoma had developed. The liver was punctured and the pathological report read "no carcinoma, only liver cirrhosis". The man returned six months later, with an implantation tumor in the puncture canal. Evidently there had been cancer cells in the materials removed with the puncture needle. The number of cancer cells in the puncture material was, however, so small that the pathologist could not recognize them. I regret to report many negative results of liver puncture in carcinoma of the liver.

Dr. Rappaport said that there was a practical difference between cholangiolitic and Laennec's liver cirrhosis because in Laennec's cirrhosis the therapy gives better results. I agree that if a patient with Laennec's liver cirrhosis has lived on a very

poor diet, high protein feeding can sometimes have an excellent effect. If a patient with Laennec's liver cirrhosis has always followed a normal diet with a satisfactory amount of proteins, then usually the results of a high protein diet are not outstanding. In cholangiolitic liver cirrhosis, I agree, there is no treatment at all.

THE GASTROINTESTINAL HORMONES*

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The secretory and motor activities of the human alimentary canal are controlled by three types of mechanism: neural, hormonal and secretagogue. My talk this afternoon is concerned with the second of these, involving the hormones, which are formed in the wall of the digestive tract for the purpose of stimulating or inhibiting one or more of the gastrointestinal functions. Such a hormone is a typical *endocrine secretion*, that is, it is formed in a specific organ, and passes into the interstitial fluid and thence into the blood stream, which transports it to some other region of the digestive tract where it exercises its particular stimulatory or inhibitory function, as the case may be. It does not act by way of the lumen of the gastrointestinal canal, in contrast with the digestive secretions which are typically *exocrine* and are poured into this lumen where they exercise their specific functions before disappearing from it. Furthermore, these gastrointestinal hormones must be differentiated from metabolic hormones like insulin and (perhaps) lipocaic, the functions of which are exercised wholly apart from the digestion processes.

The group of digestive hormones comprises at least nine distinct substances, the existence and characteristic function of which have been established in some instances but are still doubtful in others[1]. Those which have been demonstrated with more-or-less certainty are *gastrin, secretin, cholecystokinin, enterogastrone,* and *pancreozymin.* The remainder, the evidence for which is still inconclusive in varying degree, includes *enterocrinin, duocrinin, villikinin,* and *enteroanthelone.* To these, must be added *urogastrone* and *uroanthelone*—two products of urinary excretion which are always thought of in this connection even though they may not be hormones and their organ or organs of origin are not yet established.

The first of the hormones which have been definitely established is *gastrin.* This is elaborated chiefly in the antral part of the gastric mucosa but to some slight extent in the preantral region also. It is secreted into the interstitial spaces on stimulation of the prepyloric mucosa by chemical secretagogues derived from foodstuffs or by mechanical distention of the antral wall, both of which mechanisms act reflexly through local nerve endings. The actual neural processes involved here are still not clearly defined, though we know that they can be blocked by atropinization and cocainization, and that they control the secretion (and possibly formation) of the hormone, but not its action. The latter is indicated by the inability of atropine to influence the activity of exogenous gastrin, prepared by purification of an extract of the antral mucosa. The function of this hormone is to stimulate the gastric glands in the corpus and fundus of the stomach to secrete

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1. For a critical evaluation of the evidence on this point, the reader is referred to the excellent review of the subject recently prepared by M. I. Grossman, Physiol. Revs. **30**:33, (1950).

water and hydrochloric acid. It may be that it also stimulates pepsin formation, but the evidence on this at the present time is sparse.

The next, and no less important, of the well-established hormones is *secretin.* This is formed and liberated chiefly in the duodenal mucosa, but to some slight extent also in the corpus and pyloric antrum of the stomach. It is secreted particularly when hydrochloric acid in the gastric juice, bile, and a number of other substances like digested fat and soaps, are brought in contact with the mucosa of the duodenum. Neutral fats have no such secretagogue action, nor do any of the nitrogen-containing products of food digestion. The latter have been found to affect the output of secretin, but only indirectly through the stimulation of gastric secretion which, in turn, evokes the secretin mechanism in a secondary manner.

The functions of this hormone are twofold. First of all, it acts on the pancreas to stimulate the output of water and inorganic salts, particularly sodium bicarbonate. The concentration of bicarbonate in the pancreatic secretion is a function of its rate of flow; the higher the volume secreted per unit time the greater is the concentration of this salt. Secretin-stimulated pancreatic juice also contains the three pancreatic enzymes—trypsin, amylase, and lipase—but it is our belief today that these are secreted in response to stimulation by another hormone, pancreozymin, or possibly are being washed out of the pancreatic ducts by the water of the fluid secretion, rather than in response to secretin stimulation *per se.* The second function of the secretin is in relation to the liver. In this connection it exercises only a hydrocholeretic action; that is, it stimulates the output of water and inorganic salts, but not the formation or secretion of bile salts and bile pigments. Here, as in the case of the pancreas, there also obtains a distinct separation of the several functions of a single organ. So far as we know, both the pancreatic and the hepatic actions of secretin are associated with a single chemical substance. There is no evidence as yet for thinking that there exist two different secretins having different actions. It was the early idea of Bayliss and Starling, who first discovered secretin in 1902, that there might be formed in the intestinal mucosa an inactive precursor (prosecretin) which is subsequently converted into the active form. At the present time, however, there is no evidence to support this belief.

The third important member of this group of well-established hormones is *cholecystokinin.* This also is elaborated in the mucosa of the duodenum, but it has never been found in the lower small intestine or colon. Its function is to stimulate the gallbladder to contract and thus to be evacuated. The sphincter of Oddi may relax synchronously under cholecystokinin control, but this has not been established as yet. Release of this hormone can be induced by the presence of hydrochloric acid, fat, fatty acids, or peptone in the upper portion of the bowel—presumably by action on the duodenal mucosa. The nature of this action, however, has never been demonstrated, although the evidence available at present suggests that neural mechanisms are not involved in the process.

Then there is the agent, *enterogastrone.* In contradistinction to the hormones which we have already discussed, this one exercises inhibitory rather than stimulatory action, and therefore is properly classified as a chalone. It is formed in the

wall of the duodenum and jejunum, when the mucosa is stimulated with a hypertonic solution of sugar or with neutral fats, fatty acids, and especially soaps. As for the mechanism of its release, nothing whatever is known as yet. Enterogastrone has a twofold function, with considerable likelihood that it is a mixture of two different substances, in which respect it differs from secretin. The first of these functions is to inhibit the secretion of hydrochloric acid and water by the gastric mucosa; pepsin output is not affected by this hormone. The second is to inhibit all three types of muscular activity of the stomach, but only when the vagal innervation of that viscus is intact. Thus, it influences peristalsis, hunger contractions, and even the tonus level of the gastric musculature, all of which tend to diminish the propulsive force of the stomach and so increase its emptying time. On the other hand, enterogastrone has been found to induce a relaxation of the pyloric sphincter as well as the other muscles of the stomach, which tends to offset the loss of propulsive activity.

The last of this group of well-established hormones is *pancreozymin*, which also can be extracted from the mucosa of the small intestine. Its function is to stimulate the output of all three of the pancreatic enzymes. In contradistinction to secretin, it does not stimulate the output of water and bicarbonate, nor does it exercise any function so far as the liver is concerned. Consequently, when pancreozymin extract is injected into a dog with pancreatic fistula, the resulting secretion is highly viscous and very high in enzyme content, but it contains practically no bound carbonic acid.

Let us now consider those substances which I have designated merely as possibilities in this connection, because the evidence for their hormonal status is far from having been established. The first of these is *urogastrone*, which may not be a hormone at all. This is a substance, or a group of substances, which is derived from the urine of experimental animals and also of human subjects. On being injected, a purified preparation of urogastrone behaves like enterogastrone in that it inhibits both gastric secretion and gastric motility. Hence it is likely that urogastrone is also a mixture of two different substances, but the possibility that it is an excretory product rather than a hormone must still be entertained. Gastric inhibitory action is absent from the urine of hypophysectomized and oöphorectomized dogs, and since pituitrin has been found to inhibit secretion and contraction in the stomach, the suggestion was made at one time that urogastrone may originate in the pituitary or some other gland. However, subsequent evidence has forced the abandonment of this idea. There is a good possibility that the inhibitory agents derived from the urine and from the intestinal mucosa are identical, but the evidence for this is not yet complete.

Enterocrinin is another hormone which has been reported as existing in both large and small bowel. Its activity, evoked by means of a mixed meal, induces the secretion of the succus entericus from the glands of Lieberkühn throughout the entire length of the small intestine. This secretion is fluid and contains both bicarbonate and enzymes. Then there is also *duocrinin*, which has been extracted from the duodenal mucosa and is said to stimulate the secretion of Brunner's glands,

which glands occur only in the uppermost portion of the duodenum. This secretion contains a lot of mucus, and it may contain small amounts of enzymes as well, but its function in the digestive tract still remains to be determined. Duocrinin activity has been induced by dilute HCl and also various foodstuffs. Apart from these few details, little more is known about either of these reputed hormones.

A different extract prepared from the mucosa of the small intestine is said to contain *villikinin*—an agent which is believed to stimulate the motility of the villi. Such preparations increase the wavelike motion of the villi, and consequently, the rate of absorption of various foodstuffs by these minute protuberances. Whether such an extract actually contains a true hormone of this kind still remains to be proved.

This concludes the list of endocrine substances which are currently being thought of as hormones influencing secretion or motility in the gastrointestinal tract. Our subject would not be complete, however, without some mention of the substance designated *anthelone*. This substance is believed to exert a major influence in protecting the gastrointestinal mucosa against peptic ulceration in the presence of considerable quantities of active gastric juice. Evidence in support of this has been based on observations on experimental jejunal ulcers in dogs (Mann-Williamson preparations) and on spontaneous gastroduodenal ulcers in human patients. Extracts of anthelone have been prepared from the intestinal mucosa and from the urine of both men and women. Whether the purified extracts obtained from these two sources are identical or not is still an open question, and for this reason it has been proposed that they be differentiated by the names, *enteroanthelone* and *uroanthelone*, corresponding to their sites of origin in the body. It may be that the former is identical with enterogastrone and the latter urogastrone, but the evidence so far available argues against these identities.

The clinical importance of the hormones which I have presented for your consideration today, is a matter of concern to us all. Secretin has proved of considerable value as a diagnostic test agent in diseases of the pancreas and gallbladder. When pancreozymin becomes available in sufficient quantity and purity to be employed clinically, I am sure it will prove an important adjuvant in this same connection. Cholecystokinin also may be expected to prove of value diagnostically, when it has become more than a laboratory curiosity. Gastrin, on the other hand, enters into our physiological thinking in connection with the surgical management of peptic ulcer. Since gastrin is formed in the antral mucosa, the surgeons have come to believe that excision of the antrum, by reducing the output of gastric secretion, will lessen the likelihood of a recurrence of the disease, or even increase the chances of healing of an ulcer left *in situ*. Extracts of enterogastrone, urogastrone, and anthelone have been prepared in large enough quantities and in sufficiently pure state to be used for clinical trial as therapeutic agents for peptic ulcer—the two former by reducing the output of gastric juice, the latter by direct protection of the tissue. A considerable number of ulcer patients have been treated with such preparations, but the results are still indecisive.

It is evident that much remains to be learned about the gastrointestinal hormones, and it may be that ultimately they will prove to possess far more clinical importance than has been suggested by this review.

Discussion

Dr. I. Snapper:—As Dr. Hollander has said, the practical importance of these experimental results may not be evident at the present time, but the fundamental importance is very great. We have already heard this afternoon from other speakers that some investigators emphasize hormonal control of gastrointestinal functions, other scientists favor neural mechanisms. Dr. Hollander has explained that both secretin and pancreozymin act on the pancreas. One hormone leads to a secretion which can be compared to the pancreatic juice produced by stimulation of the sympathetic nerves, the other hormone produces pancreatic juice comparable to that caused by stimulation of a parasympathetic nerve.

Fundamentally then these two antagonistic mechanisms, the hormonal and the neural, are not too far apart and one day both schools of thought will have to compare notes and find a golden middle road along which they both can walk together in peace.

THE UTILITY OF ILEOCOLOSTOMY
(Mikulicz-Type)

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The present day tendency is to avoid, if possible, the performance of an ileostomy or a colostomy. For this reason the modern surgeon has accentuated primary anastomosis in colonic surgery as a preferential procedure. In some instances, however, a colostomy, for one or more reasons is inevitable. Certain pathological conditions within the abdomen may be encountered which favor the performance of a temporary ileocolostomy of a Mikulicz-type.

Since January 1950, three patients were treated surgically via a staggering ileocolostomy. It is felt that this procedure was the method of choice in the following instances.

Case 1:—Mrs. M.E.S., a fifty-eight year old housewife, was admitted to the hospital for an acute small bowel obstruction. She had a previous appendectomy and a second operation for the removal of a large right ovarian cyst. Her present obstruction, therefore, was attributed to postoperative adhesions. Roentgenograms confirmed the presence of an acute small bowel obstruction. A Miller-Abbott tube was passed into the G.I. tract prior to operation and an exploratory laparotomy was performed.

At the time of operation the small bowel was markedly dilated and difficult to manipulate. The site of obstruction was found to be in the terminal ileum where a cicatricial lesion two inches in length was found. It was thought to be a stenosing segmental ileitis. Subsequent pathological studies revealed the lesion to be an adenocarcinoma of the ileum with lymph node invasion. An adequate resection of the lesion, lymph nodes, cecum and part of the ascending colon was performed. Due to the marked distention of the small intestine a primary anastomosis of ileum to colon was not thought to be the procedure of choice. A staggering ileocolostomy (Mikulicz variety) was performed.

Case 2:—Mr. E.T., a thirty-two year old colored man, was subjected to an emergency laparotomy for an acute surgical condition within the abdomen. His history was of forty-eight hours' duration without any previous history relative to present illness. He complained of generalized abdominal pain localizing to the R.L.Q. He had nausea and vomiting. Abdominal examination indicated the presence of acute generalized peritonitis. Marked tenderness was elicited over McBurney's point. Laboratory studies revealed a W.B.C. of 19,000 with 90 per cent polys. A preoperative diagnosis of generalized peritonitis secondary to acute perforated gangrenous appendicitis was entertained.

The abdominal cavity was entered through a lower right rectus muscle-splitting incision. Generalized peritonitis was found. The site of origin was a perforated lesion in the cecum above the ileocecal valve. It was thought originally that the pathology was a perforated neoplasm of the cecum. However histological studies indicated the lesion to be a perforated diverticulum.

From the Department of Surgery, St. Peter's Hospital.

The entire ascending colon was edematous and friable. The peritoneal cavity was filled with pus. Under these circumstances the cecum, terminal ileum and a portion of the ascending colon were resected. A staggering ileocolostomy (after the plan of Mikulicz, was performed.

Case 3:—Mrs. A.I., a twenty-eight year old housewife, was admitted to the hospital for observation because of recurrent intermittent abdominal pain associated with nausea and vomiting. These episodes of pain and vomiting became more frequent and more severe. Hospitalization was suggested for study in order to determine the etiology of her complaints. At one time it was thought she had an intestinal obstruction due to postoperative adhesions. She had a cesarean section one

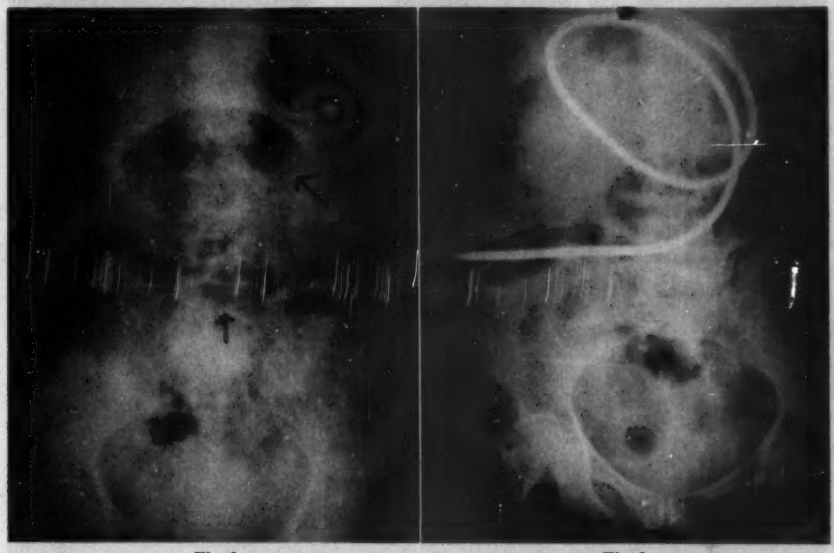

Fig. 1 Fig. 2

Fig. 1—Preoperative x-ray of patient described in Case 1 showing distended small bowel.
Fig. 2—Preoperative x-ray of same patient showing some decompression of small bowel following passage of Miller-Abbott tube.

year prior to her present hospitalization. (Postoperative adhesions do not usually form following cesarean section.)

An intensive study was made of this patient, including all types of gastrointestinal x-rays, intravenous pyelograms, etc. All failed to reveal any pathology. During this period of study she was free of symptoms. In view of the past history, it was decided to perform an exploratory laparotomy. A moderate size right ovarian cyst and a long tortuous appendix were found. Both were removed; the appendiceal stump was buried. No other pathology was found. Doubt as to the wisdom of the operation commenced to plague my mind. On the eleventh postoperative day the patient was dressed to go home. While awaiting the arrival of her husband she

developed abdominal pain, nausea and vomiting. I was contacted by telephone and advised the nurse to have the patient return to bed. One hour later I examined the patient who was comfortable and free of symptoms. The only finding was blood on the tip of the examining finger. A barium enema was given, followed by x-ray studies. This was nonrevealing.

Nothing unusual occurred during the next 24 hours. However a recurrence of symptoms commenced after 24 hours. Examination of the abdomen at this time demonstrated a palpable tender mass in the right lower quandrant. A moderate

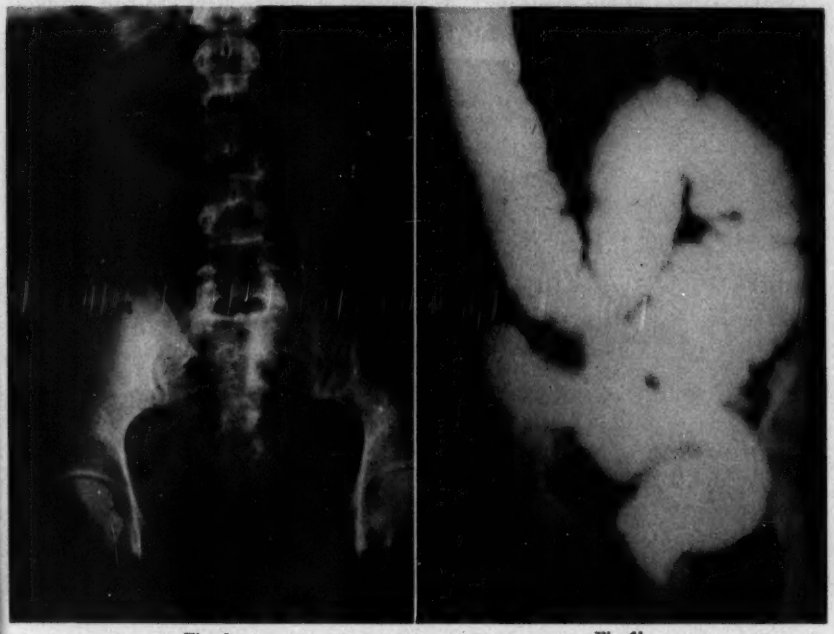

Fig. 3a Fig. 3b

Fig. 3a—Flat plate x-ray of abdomen of patient described as Case 3 showing evidence of obstruction.
Fig. 3b—X-ray of same patient following barium clysma taken 24 hours prior to flat plate in Fig. 3a.

amount of blood was eliminated rectally. A flat plate roentgenogram was taken at this time which demonstrated a small bowel obstruction.

Following adequate preoperative preparation, a second laparotomy was performed. The peritoneal cavity was filled with bloody fluid. An ileo-ileo-cecal-cecal-colic intussusception was found. The terminal ileum for 1½ feet was edematous, and pregangrenous. The cecum and ascending colon were gangrenous. It was impossible to reduce the intussusception. In order to secure a viable segment of colon, the hepatic flexure had to be liberated. After an adequate resection of the colon and ileum, a staggering ileocolostomy (Mikulicz-type) was performed.

Discussion

In the three cases presented a primary anastomosis, although possible, would be dangerous. In the presence of peritonitis, markedly dilated loops of the intestine, or with diffuse inflammatory processes of the intestine itself, primary anastomosis is not recommended. Leakage of the intestinal contents through the lines of suture is almost inevitable under these circumstances. For this reason an ileocolostomy of the Mikulicz-type is a preferable procedure.

Certain facts relative to technic are worthy of repetition at this point. In the absence of obstruction, the cut ends of the colon and ileum may be placed side-by-side at an even level on the abdomen.

In the presence of obstruction, immediate decompression may be necessary; therefore, a longer loop of ileum than colon is employed. The ileal loop should be three or four inches longer than the colon. Approximation of the ileum to the colon is performed in the usual fashion. Care must be taken to assure an adequate length so that a sufficiently long double spur will result. Adequate length of both loops will insure a deep partition, which, following the use of a crushing clamp, will provide a satisfactory opening through which the fecal stream will pass.

Sealing off the peritoneal cavity about the enterostomy occurs in forty-eight hours. When possible the laterally approximated ileum and colon should be implanted in the lower angle of the abdominal wound since this portion of the abdominal wall is movable and permits an easy freeing and closure of the enterostomy at the second operation[1].

If a long loop of ileum has been left, it may be cut away with a cautery a week following operation. Any time between ten and fourteen days the ileo-colonic partition may be broken down with a crushing clamp.

A final closure of the ileocolostomy is considered after six weeks. A longer time may be necessary for the edema (and peritonitis if present) to subside.

Summary

In the cases presented, it is felt that the procedure of ileocolostomy of the Mikulicz variety was a life-saving operation. For this reason it may be considered as the method of choice in the ileocecal area.

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A PROCTOLOGIC SURVEY OF A CHRONIC DISEASE HOSPITAL*

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Proctologists have always been aware that frequently persons who fail to offer any complaint referable to the lower bowel, are found to have anorectal abnormalities of significance. It occurred to the proctologic staff of the Jewish Sanitarium and Hospital for Chronic Diseases, to proceed with a survey of all available patients, in an effort to determine the presence of anorectal and colonic conditions that were not apparent.

Material

The great majority of the 541 patients in the hospital suffer from some incapacitating neurologic or degenerative vascular disease. Only 426, or 73 per cent, were in condition to be examined, the others being too ill. Of these 202 were males, and 224 females. Their ages ranged from 8 to 90. The majority (66 per cent) were over 50, and fully 47 per cent over 60 (Table I).

TABLE I

Sex and Ages of Patients Examined

Age	Males	Females	Total
1–9	2	–	2
10–19	4	1	5
20–29	21	12	33
30–39	18	21	39
40–49	23	44	67
50–59	43	36	79
60–69	54	55	109
70–79	31	49	80
80–89	6	4	10
90 and more	–	2	2
Total	202	224	426

The diseases represented among this group are shown in Table II. Vascular disease, including generalized arteriosclerosis, cerebrovascular accidents, hypertension and cardiac disorders, heads the list with 138 patients. Parkinsonism is second, with 116. The remaining 172 were for the most part neurologic cases.

*From the Proctologic Service of the Jewish Sanitarium and Hospital for Chronic Diseases.

TABLE II

ADMISSION DIAGNOSES OF 426 PATIENTS EXAMINED

Vascular Disease	138
Parkinsonism	116
Diabetes Mellitus	42
Chronic Arthritis	36
Multiple Sclerosis	32
Little's Disease	27
Fractures	13
Muscular Dystrophies	9
Cancer	8
Tumor, Central Nervous System	7
Amputees	6
Asthma	5
Degeneration of C.N.S.	6
Endocrinopathy	5
Mental Cases	5
Spinal Defect	4
Lues	3
Miscellaneous	18

SYMPTOMS

Though there had been scarcely any complaints referable to the lower intestinal tract, the use of leading questions readily elicited symptoms in 273 or 66 per cent of our patients:

Constipation	187
Protrusion at anus	41
Anal pain	27
Fecal incontinence	16
Rectal bleeding	16
Diarrhea	13
Pruritus	8

EXAMINATION

Since our subjects were nearly all confined to bed or wheel-chairs, it was found necessary, in the process of examination, to employ a nurse and two husky nurse-aids to transfer them to and from the examining table.

The usual preparation for examination consisted of a mild laxative (milk of magnesia or compound licorice powder) the day before, and of tap-water enemas several hours prior to call. This preparation however, failed to produce a satisfactory cleansing of the lower bowel in fully 50 per cent because of either spasm or lack of propulsive power. In many cases, consequently, it was necessary to repeat examination several times, in some as many as ten times.

Our routine consisted of palpation of the abdomen and groins, inspection of the perianum, digital examination and proctosigmoidoscopy. The left lateral (Sims') position was used in preference to knee-chest or inverted positions since the latter two usually proved impossible. Where indicated, barium colon studies were made.

Of the 426 patients examined, 32 were incompletely proctoscoped because of general spasticity or inability of effecting a proper cleansing of the bowel.

Findings

Because of the generally advanced age of the group and because of their inactivity imposed by helplessness, we expected to find a high incidence of atonia, obstipation with tendency to fecal impaction, hemorrhoids, prolapse and neoplasia. Diminished resistance to infection and the probability of trauma from enema, hard stools, rectal tubes, thermometers and digital examinations, we surmised, made likely the creation of fissures, ulcers, abscesses and fistulae. This line of reasoning was only partly borne out by our findings (Tables III, IV, and V).

TABLE III

Per Cent Incidence of Anorectal Conditions in Unselected Series of People

	A. Jewish Sanitarium and Hospital for Chr. Diseases			Group B	Group C	Group D	Group E
	Male	Female	Total				
No. examined	202	224	426	357	190	1500	1014
No. with positive findings	185	182	367				
% with positive findings	91.	81.	86.	64.	73.		
External hemorrhoids	32.7	38.	35.		49.		
Internal hemorrhoids	65.	60.	63.		22.		
Hemorrhoids			64.	36.			33.
Anal fissure, ulcer	5.4	6.	5.6	3.6	6.8	1.5	1.
Fistula			.5	8.4	6.8		
Pruritus ani	6.4	7.6	7.	2.			
Hypertrophied Papillae	16.	18.	17.	8.	11.		1.
Sphincter Spasm	12.	4.	8.				
Colospasm	11.	1.8	6.				
Impaction	5.	10.	8.				
Prolapse			1.2	.2			
Patulous Anus	4.5	7.	5.6				
Anal stricture			.7		.5	.2	
Polyp	2.	1.3	1.6	1.1		5.3	1.8
Melanosis coli			1.2				
Proctitis			8.	4.2			1.7
Colitis			.2	3.1		.3	
Cancer of rectum			.2			.3	
Amebiasis						.2	
Condylomata			.5				

Because we could find no reports of parallel studies, we have been obliged to refer for comparison to figures published in connection with proctologic surveys of the following unselected series.

B. A group of 357 male patients in the tuberculosis wards of the Kingston Avenue Hospital for Contagious Diseases[7].

C. A group of 190 males with pulmonary tuberculosis at the Glen Lake Sanitorium[9].

D. A group of 1,500 apparently healthy women[10].

E. A group of 1,014 women, ages 22 to 74, who considered themselves well[8].

Positive proctologic findings were noted in 367, or 86 per cent of the patients examined by our group as against 65 per cent and 73 per cent in group B and C, respectively (Table III). Their frequency was higher among males, 91 per cent as against 81 per cent among females. The outstanding disparities between the sexes were found in the incidence of the following conditions: Sphincter spasm in 12 per cent of male patients and only 4 per cent in the females. Colospasm, too, was a much more frequent occurrence among males (11 per cent against 1.8 per cent). On

TABLE IV

INCIDENCE OF ANORECTAL CONDITIONS WITHIN AGE-GROUPS

	Ext. Hemorrhoids	Int. Hemorrhoids	Pruritus	Fissure	Papillitis	Sphincter Spasm	Colospasm	Impaction	Proctitis	Prolapse	Patulous Anus	Stricture	Polyps	Total Examined
Age														
1–9	0	1	0	0	0	1	0	0	0	0	0	0	0	2
10–19	0	0	0	1	0	0	0	0	0	0	0	0	0	5
20–29	7 21%	17 52%	0 0	1 3%	2 6%	9 27%	5 15%	3 9%	0 0	0 0	0 0	0 0	0 0	33
30–39	12 31%	23 60%	3 8%	2 5%	5 12%	3 8%	3 8%	3 8%	3 8%	0 0	1 3%	0 0	0 0	39
40–49	22 33%	34 50%	6 9%	5 7%	9 19%	6 9%	1 1.5%	3 4%	3 4%	0 0	1 1.5%	0 0	1 1.5%	67
50–59	38 50%	61 78%	8 10%	6 8%	16 20%	4 5%	5 6%	5 6%	10 12%	1 1%	4 5%	1 1%	0 0	79
60–69	43 39%	81 74%	10 9%	3 3%	28 26%	4 4%	7 6%	13 12%	9 8%	2 2%	12 11%	2 2%	5 5%	109
70–79	25 31%	45 56%	2 2.5%	4 5%	12 15%	6 7.5%	5 6%	4 5%	8 10%	2 2.5%	5 6%	0 0	1 1%	80
80–89	4 40%	6 60%	1 10%	2 20%	1 10%	0 0	1 10%	2 20%	0 0	1 10%	1 10%	0 0	0 0	10
90 & more	0	0	0	0	0	0	0	1	0	0	0	0	0	2
Total No. %	151 35.	268 63.	30 7.	24 5.6	73 17.	34 8.	27 6.	34 8.	33 8.	6 1.2	24 5.6	3 .7	7 1.6	426 100

the other hand, impaction was found twice as often among the females as among the males (10 per cent as against 5 per cent), and patulous anus was present in 7 per cent of our female patients, but in only 4.5 per cent of the males.

In the succeeding discussion of the various rectal conditions, each taken individually, unless otherwise referred to, Table III should be consulted with reference to incidence within sex groups, Table IV within age groups, and Table V within disease groups.

TABLE V

INCIDENCE OF ANORECTAL CONDITIONS WITHIN EACH DISEASE-GROUP

		Parkinsonism	Vascular Disease	Chronic Arthritis	Little's Disease	Multiple Sclerosis	Diabetes	Muscular Dystrophy	CNS Degeneration	Miscellaneous Dis.	Total
Total No.		116	138	36	27	32	42	9	6		426
External Hemorrhoids	No.	44	56	12	5	10	10	3	3	21	151
	%	38.	40.	33.	18.	31.	24.	33.	50.		35.
Internal Hemorrhoids	No.	71	76	24	15	19	22	5	3	32	268
	%	61.	55.	66.	55.	60.	52.	55.	50.		63.
Pruritus Ani	No.	9	13	2	1	0	3	0	0	4	30
	%	8.	9.	6.	4.	0	7.	0	0		7.
Fissure	No.	9	5	0	3	2	3	0	0	2	24
	%	8.	3.6	0	11.	6.	7.	0	0		5.6
Fistula	No.	0	0	1	0	0	0	0	0	1	2
	%	0	0	3.	0	0	0	0	0		.5
Condylomata	No.	0	2	1	0	2	1	0	0	0	2
	%	0	1.5	3.	0	6.	3.	0	0		.5
Hypertrophied Papillae	No.	27	20	8	3	4	6	0	2	6	73
	%	23.	14.	24.	11.	12.	14.	0	33.		17.
Sphincter Spasm	No.	8	4	2	5	2	4	4	1	4	34
	%	7.	3.	6.	18.	6.	10.	44.	16.		8.
Colospasm	No.	4	7	0	3	3	4	2	2	3	27
	%	3.5	5.	0	11.	9.	10.	22.	33.		6.
Impaction	No.	9	11	0	2	1	6	0	2	4	34
	%	8.	8.	0	8.	3.	14.	0	33.		8.
Prolapse	No.	0	2	1	0	0	1	0	0	2	6
	%	0	1.5	3.	0	0	2.	0	0		1.2
Patulous Anus	No.	6	4	3	0	1	3	0	0	6	24
	%	5.	3.	8.	0	3.	7.	0	0		5.6
Stricture	No.	1	2	0	0	0	0	0	0	0	3
	%	1.	1.5	0	0	0	0	0	0		.7
Polyps	No.	2	3	0	0	0	2	0	0	1	7
	%	2.	2.	0	0	0	5.	0	0		1.6
Proctitis	No.	8	8	3	1	2	4	0	2	5	33
	%	7.	6.	8.	4.	6.	10.	0	33.		8.
Melanosis	No.	1	3	2	0	0	0	0	0	0	6
	%	1.	2.	6.	0	0	0	0	0		1.2

Hemorrhoids

External hemorrhoids were found in 151, or 35 per cent of our patients. With the exception of 6, these were associated with internal hemorrhoids. They were slightly more common among the females (38 per cent as against 32.7 per cent among males). Their frequency increased gradually with age, being highest in those between 50 and 59 (50 per cent). Of the disease-groups, those with vascular disorders showed the highest tendency (40 per cent).

Internal hemorrhoids were present in 268 (63 per cent of those examined), 65 per cent of the male patients and 60 per cent of the females. They were most common in the 5th and 6th decades (76 per cent). As for disease-groups, the arthritics showed the greatest predilection (66 per cent).

These figures point to a considerably higher incidence of internal hemorrhoids among our patients, than among the three series employed for comparison (Table III). This was, of course, as expected, considering that most of our patients were inactive, constipated, elderly people, who would naturally be subject to venostasis in the anal region.

Fissures

Fissures were noted in 24, or 5.6 per cent—6 per cent among the females, 5.4 per cent among the males. The distribution as to age was uneven, without a definite pattern. Fully 11 per cent of the patients with Little's Disease had this condition, this incidence being the highest among the disease-groups. In comparison with the other recorded series, our figure for fissures is higher than some, but not as high as others (Table III).

Pruritus

Thirty, or 7 per cent of our patients showed evidence of chronic pruritus ani. The females showed an incidence of 7.6 per cent, the males 6.4 per cent. All were over 30 years old. The highest frequency was found in the 5th decade (10 per cent). Of the disease-groups, vascular diseases were first, with 9 per cent, trailed by Parkinson's Disease with 8 per cent. Strangely enough, only three out of 42 diabetics had pruritus ani, an incidence of only 7 per cent, the same as for the entire group.

For comparison, the study of a group of patients in a tuberculosis hospital showed pruritus to be present in only 2 per cent.

Among the anorectal conditions associated with our cases of pruritus, we found hemorrhoids in 47 per cent, hypertrophied papillae in 30 per cent, and cryptitis in 10 per cent.

Hypertrophied Papillae

Hypertrophied anal papillae were found in 73, or 17 per cent of our series, almost equally distributed as to sex. Of the disease-groups, those with Parkinsonism and arthritis showed the greatest frequency,—23 per cent and 24 per cent, respectively. They were most common in patients in the 6th decade (26 per cent). Ten per cent of patients with hypertrophied papillae had pruritus ani, compared with 7 per cent in our series as a whole.

The frequency of hypertrophied papillae in other chronic disease-groups is considerably lower (8 per cent and 11 per cent as against 17 per cent) (Table III).

Patulous Anus

A relaxed sphincter ani with a patulous anus was noted in 24, or 5.6 per cent of this series,—more frequently in females than in males (in 7 per cent of the former as against 4.5 per cent in the latter). The diabetics and arthritics showed the highest incidence among the disease-groups,—7 per cent and 8 per cent respectively. It was most common among those past 60 (9 per cent). Associated with this condition were: hemorrhoids in 20 of the 24 patients, fecal impaction in 2 and colospasm in 2.

Prolapse

Rectal prolapse presented itself in only 6, or 1.2 per cent, about equally distributed as to sex. The youngest patient was 50 years old. All were mucosal-type prolapses, no procidentia being encountered.

In comparison, the tuberculosis wards of the Kingston Avenue Hospital showed an incidence of only 0.2 per cent. The difference can apparently be explained by the much higher age average of our group.

Impaction

Severe fecal impaction was encountered in 34, or 8 per cent of our patients, and twice as frequently among the females as among the males (10 per cent and 5 per cent respectively). This difference is explainable by the lesser muscular development in females, as well as flaccidity that follows repeated childbirths. Three of these patients were found to have a narrowing of the anal canal from previous surgical procedures: one following fistulectomy and two following hemorrhoidectomy. Every third patient with central nervous system degeneration presented this syndrome. Impaction was encountered with the greatest frequency in the older groups,—in 10 per cent of patients over 60.

Sphincter Spasm

Spasm of the anal sphincters was evident in 34, or 8 per cent of the series. It was most predominant in males (in 12 per cent, as against 4 per cent in females). The patients affected were mostly in the younger groups. Fully 27 per cent of those between 20 and 29 had sphincteric spasm, while among patients over 50, only 5 per cent showed this condition. Patients having muscular dystrophy showed the highest percentage (44 per cent). The next highest frequency was found among those with Little's Disease (18.5 per cent). Of the rectal conditions associated with sphincter spasm, the following were most common: Hemorrhoids in 56 per cent, cryptopapillitis in 29 per cent, colospasm in 24 per cent, and fissures in 15 per cent.

Colospasm

Appreciable spasm of colon or rectosigmoid was noted in 27, or 6 per cent of the series. It was several times more frequent among the males than females, 11 per cent as compared to 1.8 per cent. Colospasm was most prevalent in the 20 to 29 year group (15 per cent). Little's Disease, diabetes and multiple sclerosis showed

an incidence of 11 per cent, 10 per cent, and 9 per cent respectively. Two of our six patients with degeneration of the central nervous system showed this condition. It is therefore evident that the greatest incidence of colospasm was to be found amongst those with neurologic disease.

Of the 27 patients with colospasm, there was an associated sphincter spasm in 8, proctitis in 5, and a patulous anus in 2. Both colospasm and sphincter spasm were present in the following: Two patients with Parkinsonism, one with Little's Disease, one with multiple sclerosis, and one with muscular dystrophy. On the other hand, colospasm with a patulous anus was present in one patient with Parkinsonism and one with multiple sclerosis.

TABLE VI

INCIDENCE OF RECTAL POLYPS IN VARIOUS SERIES

Observer	No.	Composition	Examination	Patients with Polyps	% Polyps
Marino, et al[7]	357	Male, TB	Proctoscopy	4	1.1
Binkley[2]	2912		"	188	6.4
Steele & Brown[10]	1500	Healthy	"	79	5.3
Ortmayer & Connelly[8]	1014	Healthy women	Proctoscopy 20 cm.	19	1.8
Stewart[11]	1815	63% male	Autopsies	76	4.2
Sussman[12]	1100		"	66	6.
Swinton[13]	1843		"		7.
Helwig[5]	1460		"	139	9.5
Atwater & Bargen[1]	241		"	166	69.
Lawrence[6]	7000	Ages 32-56	"	166	2.4
Fansler[4]	256	Normal	Proctoscopy	38	14.9
Buie[3]	910	Normal	"	76	8.4
Authors	426	Chronic Diseases	Proctoscopy 20 cm	7	1.6

The high incidence of sphincter spasm and colospasm in the younger patients may perhaps be explained by the prevalence of spasm in the disease-groups affecting the younger people such as Little's Disease and multiple sclerosis.

RECTAL POLYPS

Polyps were discovered in only 7 of our patients, or in 1.6 per cent of the series. This is surprisingly low when we compare the findings of other observers (Table VI).

In one of our patients there were at least 4 polyps. The others had only one each. The incidence in males was found to be 2 per cent, as against 1.3 per cent in females. This greater predisposition in males corresponds with the findings of several other observers[2,6,11,13].

Of the 7 patients with polyps, 6 were between 60 and 79 years of age. A progressive increase with advance in age is shown by the observations, in thousands of cases, by other authors[5,12] (Table VII).

The polyps were situated from two to six inches from the anorectal line, except for two in the colon of one patient, which were discovered with the aid of a barium enema. The sizes were from pea-size to a half-inch in diameter. The symptoms complained of were constipation in six of the seven patients. None of them complained of bleeding. One patient, who had the lowest situated polyp, complained of pain. Carcinomatous degeneration was discovered in only one of the five polyps which were examined microscopically.

Summary

In a chronic disease hospital, with the great mass of patients suffering from incapacitating vascular or nervous disease, it was possible to perform a proctologic survey in 426 out of 541 patients, without mishap.

In spite of a paucity of offered complaints, 86 per cent of our series showed the presence of abnormal anorectal conditions. In general, the incidence was higher among males than females. Women seemed particularly more prone to have relaxation of the anorectum, while the male showed a higher incidence of spastic conditions and polyps. There was a high incidence of hemorrhoids, hypertrophied papillae, proctitis, fecal impaction, sphincter spasm, colospasm, pruritus ani and fissure.

Polyps, although found less frequently among our patients as compared with other series in routine surveys, still represent an important result of our study, because of the implication inherent in their presence, i.e., the development of malignancy as shown in one of our cases.

Only two patients were found to have a fistula-in-ano.

We failed to find abscesses, pilonidal cysts, venereal lesions, megacolon, ulcerative colitis or tuberculosis. With the exception of one of the cases with a well-healed abdominoperineal resection and that of the malignant polyp noted, there were no cases of carcinoma of the rectum.

TABLE VII

Incidence, in Per Cent, of Polyps Among Age-Groups

Years	Group A No. of Pts. Examined	Group A % with polyps	Group F % with polyps	Group G % with polyps
1-9	2	0	0	2.5
10-19	5	0	0	1.3
20-29	33	0	.9	0
30-39	39	0	2.9	8.2
40-49	67	1.5	5.2	7.9
50-59	79	0	7.2	16.
60-69	109	5.	13.7	21.2
70-79	80	1.5	8.7	24.2
80 plus	12	0	—	16.6

Group A — 426 patients at the Jewish Sanitarium and Hospital for Chronic Diseases
Group F — 1,100 autopsies
Group G — 1,460 autopsies

Conclusions

Even though this survey was time consuming, we feel well justified by the results obtained. They show that even though the history may not point to the anorectum, a complete proctologic examination should be included in the routine examination in each case upon admission, and repeated at regular intervals.

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A NEW MODIFICATION OF THE HEMOGLOBIN TECHNIC FOR THE DETERMINATION OF PEPSIN IN GASTRIC JUICE ADAPTED FOR A WIDE RANGE OF VALUES

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Interest in peptic digestion has led to the development of several methods for the quantitative estimation of pepsin in the gastric juice[1-11]. The Anson-Mirsky method[8,9], based on the digestion of hemoglobin, is one of the most satisfactory. Its advantages include the use of a stable reproducible substrate and a relatively precise colorimetric reaction[12]. The method is not accurate, however, in the high range of pepsin concentration because of the failure of full proteolytic activity to occur in the presence of pepsin inhibitors. The original hemoglobin method has been variously modified in an attempt to increase its range of applicability[13-16]. Currently the most widely used modification is that of Bucher, Grossman and Ivy, who minimized by dilution the problem of pepsin inhibitors[16].This maneuver, however, multiplies the possibility of encountering pepsin values outside the optimal concentration for the colorimetric reaction.

The Bucher et al. method[16] can be used only if the color values of the filtrate fall in the range between 3 and 11 mEq. x 10^{-4} tyrosine, since the values below 3 mEq. x 10^{-4} are unreliable according to the authors, and for those above 11 mEq. x 10^{-4} no equations are given. Since the standard dilution of 1:100 is used, this dilution will be good only for pepsin concentrations ranging from 170 to 800 PU. These values are, however, rather high, because in man the pepsin values in many instances, especially in fasting gastric juice, may be much below this range[17]. Under these circumstances an additional dilution of gastric juice to 1:25 or less would be required, thus increasing the labor of the test.

The present communication describes a new modification which attempts to resolve the difficulty of containing the reaction within the optimal range of available photoelectric colorimeters and to increase the relatively narrow range of the Anson-Mirsky calibration curve. By increasing the quantity of gastric juice tested, changing the ratio of hemoglobin substrate to the material containing pepsin, and varying the concentration of reagents used in the Folin-Ciocalteu reaction it was possible to set a new calibration curve for pepsin, which circumvents the difficulties mentioned, and which is accurate over the entire physiologic and pathologic range within 5 per cent.

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Any colorimeter can be used for this modification, provided that it is precalibrated for the Folin-Ciocalteu reaction at concentrations of reagents used, and for the entire possible range of tyrosine values. We selected the Rouy-Leitz photrometer which contains an optical system based on Rouy's modified equation for photonic energy absorption[18] and which we have precalibrated for the entire range of tyrosine concentrations which might be encountered.

The precalibration of the instrument was done with recourse to Rouy's data. The most suitable filters were determined by testing the full range of tyrosine concentrations, which might be encountered, and calculating the smallest positive or largest negative "cut off residual"[18]. The most suitable filter for the Folin-Ciocalteu reactions with this photrometer was found to be the red filter (640 millimicrons) for low and medium tyrosine values (above the reading of 20.0 on the scale of the photrometer, i.e. below 334 micrograms of tyrosine), and a blue filter (415 millimicrons) for high tyrosine values (below 20.0 readings on the scale of the apparatus,

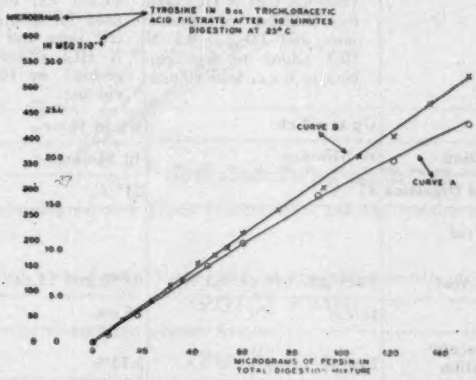

Fig. 1—Curve A represents the failure of complete digestion of the hemoglobin substrate in the presence of relatively high concentration of pepsin in the digestion mixture. Consequently the curve deviates below the straight line relationship (Curve B) observed when the volume of solution and the concentration of the constituents are slightly altered as suggested.

i.e. above 334 micrograms of tyrosine). With these filters in quadruplicate samples the deviation from mean values of all samples was not greater than 2 per cent.

Extension of the Peptic Activity Scale:—In the presence of a relatively high pepsin concentration the ratio of pepsin to hemoglobin substrate as used by Anson-Mirsky[8,9] is not the optimal one for the development of full peptic activity. The curve describing the increase in split products of hemoglobin as measured by the Folin-Ciocalteu reaction in the trichloracetic acid filtrate no longer followed a straight line, but tended to deviate downwards as shown in Figure 1 (Curve A). In the presence of relatively low pepsin concentration on the other hand, the readings were inexact, if a gastric juice dilution to 1:100 was used. In Table I is outlined a procedure which makes a compromise among all requirements of the technic and

is satisfactory for the widest possible range of values. As a result of this modified technic the curve of peptic activity described a straight line (Fig. 1, Curve B).

Curves of Proteolytic Activity of Crystallized Pepsin:—To determine the applicability of the above described modification of the technic for the wide range of pepsin values, several curves of proteolytic activity of several batches of commercial crystallized pepsin (Armour) were determined. This pepsin from porcine

TABLE I

	Bucher-Grosman-Ivy[15] Modification of the Hemoglobin Method	Our Modification of the Hemoglobin Method
Digestion Mixture		
Gastric Juice	0.01 c.c. (1 c.c. 1:100)	0.025 c.c. (5 c.c. 1:200)
Hemoglobin Solution	0.1 gm. (4 c.c. 2.5% sol.)	0.1 gm. (4 c.c. 2.5% sol.)
Hydrochloric Acid	0.051 N Final Concentr. (0.99 c.c. 0.01 N HCl used for dilution of gastric juice and 1.0 c.c. 0.3 N HCl added to hemoglobin) in 6 c.c. final volume	0.050 N Final Concentr. (4.975 c.c. 0.04 N HCl used for dilution of gastric juice and 1.0 c.c. 0.3 N HCl added to hemoglobin) in 10 c.c. final volume.
Water	Up to 6.0 c.c.	Up to 10 c.c.
Time of Digestion	10 Minutes	10 Minutes
Temperature of Digestion	25° C.	25° C.
Trichloracetic Acid Precipitation		
Trichloracetic Acid	0.049 gm. (10 c.c. 0.3 N)	0.050 gm. (5 c.c. 10%)
Final Volume	16 c.c.	15 c.c.
Final Trichloracetic Acid Concentration	3.06%	3.33%
Folin-Ciocalteu Reaction		
Filtrate	5 c.c. (5/16 of digestion mixture)	5 c.c. (1/3 of digestion mixture)
Sodium Hydroxide	10 c.c. 0.5 N (0.277 N Final Concentr.)	10 c.c. 0.75 N (0.300 N Final Concentr.)
Phenol Reagent	1.0 c.c. (3 c.c. 1/3 diluted) (5.55% Final Concentr.)	1.5 c.c. (6.00% Final Concentr.)
Water	Up to 18 c.c.	Up to 25 c.c.

gastric mucosa was recovered by Northrop's crystallization method from alcohol[19], and it contained, according to the communication of the producer[20], ash—less than 2.5 per cent, moisture—less than 5.0 per cent, nitrogen content 13.5 per cent, potency in national Formulary units 1:60,000, potency in proteolytic units referred to the protein nitrogen (so-called specific proteolytic activity ($PU \frac{Hb}{PN}$) = 0.22), corresponding to about 0.03 PU^{Hb} per 1 mg. pepsin.

From several batches of this pepsin product stock solutions were prepared, each containing 15 mg. of dried pepsin in 500.0 ml. of 1/20 N hydrochloric acid. From each of these stock solutions several sample solutions were prepared by the addition of water so that the final concentration of pepsin in 5 ml. ranged from 0.006 to 0.150 mg. To each of these sample solutions hemoglobin substrate was added and the entire procedure of proteolytic digestion, trichloracetic acid precipitation, filtration, development of color by Folin-Ciocalteu reaction, and reading in the Rouy-

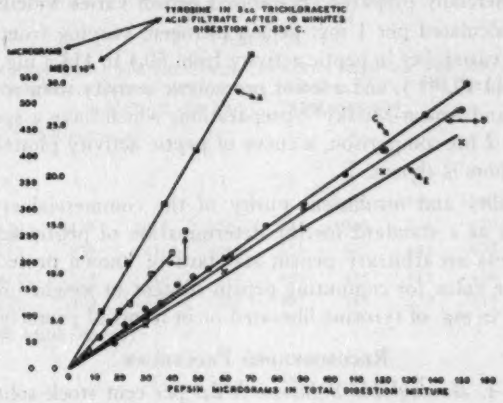

Fig. 2—Linear relationship between pepsin concentration and the tyrosine content in the digestion mixture.

A. Calculated from Anson-Mirsky data on crystalline pepsin of specific activity:
$$(PU)^{Hb}_{PN} = 0.184$$

B. Commercial crystallized pepsin, Armour.
$$(PU)^{Hb}_{PN} = 0.123$$

C. Same product, different sample.
$$(PU)^{Hb}_{PN} = 0.079$$

D. Same product, different sample.
$$(PU)^{Hb}_{PN} = 0.074$$

E. Same product, different sample.
$$(PU)^{Hb}_{PN} = 0.065$$

Leitz photrometer was performed according to the procedure outlined in Table I. All determinations were performed in duplicate, and the control tyrosine values, ($T_{con.}$) as described in the procedure below, were deducted from each tyrosine value of the filtrate of digestion mixture ($T_{dig.}$). The results, representing the correlation between the pepsin concentration in the digestion mixture and the amount of color given by split products of peptic digestion of hemoglobin ($T_{diff.} = T_{dig.} - T_{con.}$) are illustrated graphically in Figure 2 which shows a straight linear relationship between the concentration of pepsin in the digestion mixture and the amount of formed

split products of hemoglobin. This linear relationship allows a simple calculation of pepsin concentration in terms of tyrosine content in the trichloracetic acid filtrate.

The accuracy of the method was calculated by computing the standard error of the duplicate points from the means represented by the calibration curve of proteolytic activity reproduced in Figure 2. The average standard error was found to be 5 per cent.

From the data listed in Figure 2 it is clear that the peptic activity of various batches of commercially prepared crystallized pepsin varies widely, specific activities (PU^{Hb}_{PN}), calculated per 1 mg. pepsin nitrogen, varying from 0.123 to 0.065. This indicates a variability in peptic activity from 60.4 to 113.5 mg. pepsin for each proteolytic unit (1 PU^{Hb}), and a lower proteolytic activity than specified and than the Northrop[21] and Anson-Mirsky[8,9] preparations which have a specific activity of 0.184. In Figure 2 for comparison, a curve of peptic activity plotted from the data of the latter authors is shown.

The variability and insufficient purity of the commercial crystalline pepsin precludes its use as a standard for the determination of peptic activity of gastric juice. Thus, unless an arbitrary pepsin standard of known proteolytic activity is used as reference value for computing pepsin content in weight units, one can express the results in mg. of tyrosine liberated or in terms of proteolytic units.

Recommended Procedure

Reagents:—1. *Hemoglobin Solution.* A 2.5 per cent stock solution in water is prepared from Bovine Hemoglobin Enzyme Powder (prepared for Anson-Mirsky proteolytic methods)—Armour. This may be stored in the refrigerator after adding 1 mg. merthiolate for each 40 ml. of hemoglobin solution. From this stock solution hemoglobin substrate is prepared on the day of the determination by adding ¼ volume of 0.3 N HCl for each volume of hemoglobin stock solution.

2. *Folin-Ciocalteu Phosphotungstic-Phosphomolybdic Phenol Reagent* which may be bought ready made.

3. *0.04 N Hydrochloric Acid.*

4. *0.3 N Hydrochloric Acid.*

5. *3 Per cent (0.75 N) Sodium Hydroxide.*

6. *10 Per cent Trichloracetic Acid.*

Equipment:—Photoelectric colorimeter; water bath at 25°C.; test tubes, pipettes, test tubes having a mark at 25 ml., volumetric 200 c.c. flasks, Whatman No. 50, 11 cm. filter paper.

Procedure:—One ml. of centrifuged and filtered gastric juice is placed into a 200 ml. volumetric flask. The latter is filled with 0.04 N HCl to the 200 ml. mark, and the contents mixed. Five ml. of this diluted gastric juice are measured into a test tube and placed into the water bath at 25°C. Five ml. of the hemoglobin substrate containing 4 ml. of hemoglobin and 1 ml. of 0.3 N HCl solution are added and the contents of the tube mixed thoroughly by whirling the tube without removing it from the water bath. The digestion is continued for exactly 10 minutes (stop-

watch) while the temperature of the bath is maintained carefully at 25°C. After exactly 10 minutes 5 ml. of 10 per cent trichloracetic acid are added, the tube is removed from the bath, the contents are mixed by inversion and the tube is left standing for 5 to 10 minutes at room temperature.

During this time a control is prepared by measuring into another test tube in sequence 5 ml. of 1:200 gastric juice, 5 ml. of 10 per cent trichloracetic acid and 5 ml. of the hemoglobin substrate. The contents of the tube are mixed by inversion and left standing for 5 to 10 minutes at room temperature.

TABLE II

CALIBRATION TABLE FOR THE FOLIN-CIOCALTEU REACTION AND ROUY-LEITZ PHOTROMETER, AS USED IN THE ACTUAL MODIFICATION OF THE HEMOGLOBIN METHOD FOR PEPSIN DETERMINATION

Blue Filter (415 Millimicrons)

Meter Reading*	0	1	2	3	4	5	6	7	8	9
0						1600	1480	1380	1300	1230
10	1170	1115	1065	1020	978	940	904	870	838	808
20	780	754	730	708	686	665	643	623	603	584
30	565	547	530	514	499	485	472	459	446	433
40	420	408	397	387	377	368	359	350	341	332

Red Filter (640 Millimicrons)

Meter Reading*	0	1	2	3	4	5	6	7	8	9
0										
10										
20	334	323	313	304	296	288	281	274	267	260
30	254	247	241	235	229	223	217	211	205	200
40	195	190	185	181	176	171	166	162	157	153
50	148	144	140	135	131	127	123	120	116	113
60	109	106	102	99	95	92	89	86	83	80
70	77	74	71	69	66	63	60	57	55	52
80	49	46	44	41	39	36	33	31	28	26
90	23	21	18	16	13	11	9	7	4	2

*The numbers in the center of the table (from 2 to 1600) correspond to tyrosine micrograms in 25 c.c. mixture of tyrosine solution, Folin-Ciocalteu reagent, and alkali.

The meter reading from 0 to 9 in the horizontal line should be added to the meter reading of the vertical line, e.g. 20 + 2 reading (i.e. 22) equals 313 micrograms of tyrosine if red filter is used.

Now, the contents of both test tubes, containing digestion mixture and control, are filtered through Whatman No. 50, 11 cm. filter paper. Five ml. of each of the two filtrates are transferred into test tubes having a mark at 25 ml. volume, and to each of these two samples 10 ml. of 3 per cent (0.75 N) NaOH and 1½ ml. of Folin-Ciocalteu reagent are added. The tubes are filled with distilled water up to the 25 ml. mark. The contents are mixed by inversion and left standing unstoppered in a rack for 10 minutes at room temperature.

In the meantime a blank is prepared by adding to 5 ml. of distilled water, 10 ml. of 3 per cent sodium hydroxide, 1½ ml. of phenol reagent and again filling with

water up to the volume of 25 ml. The blank is set in the photoelectric cell and the reading of the blank is made using the red filter. In case of the Leitz photrometer the needle of the meter is set at 100 while the blank is in the cell. The blank is removed, and starting at least 10 and not later than 20 minutes after the addition of the reagents, the photoelectric readings of both (digested and control) solutions are taken one after another. If the color density is so great that with the red filter the reading falls in the low range of values (below 20 with Leitz photrometer) the filter is replaced by a blue one, and a new reading is made and used for calculation. The method is suited for serial determinations so that up to 12-15 specimens of gastric juice may be examined at once. The range of the present modification includes from 2.5 to 1,920.0 proteolytic units, if calculated at 35.5°C., and from 1.5 to 1,055.0 proteolytic units if calculated at 25°C. The photoelectric colorimeter must be precalibrated for tyrosine concentrations of a range from 2 to 1,600 micrograms in 25 ml. mixture of tyrosine solution, Folin-Ciocalteu reagent and alkali, and the red filter must be used for concentrations below 334 micrograms, the blue one for those above 334 micrograms of tyrosine.

Calculations:—The colorimetric readings of both filtrates (digestion mixture and control) are converted into micrograms of tyrosine on the basis of calibration data of the colorimeter used. Since no precalibration data of the Folin-Ciocalteu reaction were available for the Rouy-Leitz photrometer, our respective precalibration figures are listed in Table II for current use with this apparatus.

From the tyrosine value in micrograms of the filtrate of digestion mixture ($T_{dig.}$) the tyrosine value in micrograms of the filtrate of control ($T_{con.}$) is deducted. The difference in micrograms ($T_{diff.}$) represents the amount of tyrosine in solution which, with Folin-Ciocalteu reagent under standard conditions, yields the color equivalent to that which is obtained from the split products of peptic digestion of the hemoglobin substrate present in 5 c.c. of filtrate after 10 minutes digestion at 25°C.

This value is converted into proteolytic units at 35.5°C.[8,9] by expressing the $T_{diff.}$ in milliequivalents, instead of micrograms (dividing it by 181,000) and calculating it for 1 minute of digestion (dividing it by 10), for total volume of digestion mixture (multiplying by $\frac{15}{5}$) and for digestion temperature of 35.5°C. (multiplying it by 1.82)[9], and finally taking into account the dilution factor and volume of the gastric juice used (multiplying by $\frac{200}{5}$).

Hence:—

(1) PU^{Hb} in 1 ml. gastric juice $= \frac{(T_{dig.} - T_{con.}) \times 15 \times 1.82 \times 200}{181 \times 1000 \times 10 \times 5 \times 5} = \frac{T_{diff.} \times 1.207}{10^4}$ or

(2) $PU^{Hb} \times 10^4$ in 1 ml. gastric juice $= T_{diff.} \times 1.207$

Example:—Reading of the 5 ml. filtrate of the digestion mixture: 63.5, with filter 640 and Leitz photrometer; reading of the 5 ml. filtrate of the control: 84.0 with the same filter; $T_{dig.} = 97$; $T_{con.} = 39$; $T_{diff.} = 58$; PU^{Hb} in 1 ml. g.j. $= 0.0070$; $PU^{Hb} \times 10^4$ in one ml. g.j. $= 70$.

It must be emphasized that these proteolytic units refer to digestion temperature of 35.5°C., and that 1.82 of these proteolytic units will equal 1.0 proteolytic unit calculated at 25°C.

To facilitate the determination of the mutual secretory interrelationship of pepsin to various gastric juice constituents (HCl, chlorides, mucoprotein and mucoproteose)[17] it might be convenient to express pepsin in the same gravimetric units as used for determination of the other components of gastric secretion. This way of calculation is possible only by an arbitrary selection of a crystallized pepsin product as an abstract standard of conversion value from proteolytic units into weight units, e.g. by arbitrary selection of the crystalline Northrop-Anson-Mirsky pepsin of specific activity 0.184[8,9,21] as a basis for conversion.

Since the average nitrogen content of this crystalline pepsin[22] is 15.3 and its specific activity is 0.184, the PU^{Hb} of 1 mg. of this pepsin would be 0.02815, which means that

(3) Pepsin mg. in 100 ml. gastric juice $= \frac{T_{diff.} \times 1.207 \times 100}{10^4 \times 0.02815} = T_{diff.} \times 0.429$ or

(4) Pepsin mg. in 100 ml. g.j. = Pepsin in $PU^{Hb} \times 10^4$ in 1 ml. g.j. x 0.355

It must be emphasized that this way of conversion reports the peptic activity of gastric juice in mg. of pepsin of a specific activity of 0.184. It is obvious that no true weight values for pepsin content can be thus obtained, because neither the peptic activity of pure pepsin nor the amount of inactivated or inert pepsin in solution is known. Because of this limitation the reporting of the results in micrograms tyrosine liberated on digestion ($T_{diff.}$), or better in terms of PU^{Hb} in 1 ml. gastric juice are preferable.

Summary

A modification of the Anson-Mirsky hemoglobin method for the determination of pepsin in gastric juice is described. Its chief advantage lies in the fact that it covers the widest possible range of pepsin values. This modification may be used with any colorimeter, after its precalibration for the Folin-Ciocalteu reaction, as used in the particular technic described, and for the range of tyrosine concentrations between 2 and 1,600 micrograms in 25.0 ml. of solution. Respective precalibration data for the Rouy-Leitz photrometer are supplied.

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NEWS NOTES

Sixteenth Annual Convention

The program for our Sixteenth Annual Convention will be found in this issue of The Review of Gastroenterology.

Copies are being mailed out separately to members of the Association and additional programs are available from the headquarters office, 1819 Broadway, New York 23, N. Y. The program will also be available at the registration desk on the convention floor.

This year, following the enthusiastic reception accorded the last evening meeting, another evening session has been scheduled for Wednesday, 19 September 1951.

The convention sessions are open to the general medical public.

Registration

Those attending the convention are requested to register and receive their identification badges. Ladies are also invited to register. No one will be admitted to the exhibits or the sessions without a badge.

Annual Meeting of the National Council

The Annual Meeting of the National Council of the National Gastroenterological Association will be held at The Drake in Chicago, Ill. on Sunday afternoon, 16 September 1951 at 4:00 P.M.

Following the meeting of the Council there will be a banquet for the officers and members of the Council.

Annual Meeting of the National Executive Committee

The Annual Meeting of the National Executive Committee will be held at The Drake in Chicago, Ill., at 3:00 P.M. on Sunday afternoon, 16 September 1951.

Annual Meeting of the National Gastroenterological Association

The Annual Meeting of the National Gastroenterological Association will be held at The Drake in Chicago, Ill., at 4:00 P.M. on Monday, 17 September 1951, the first day of the Sixteenth Annual Convention. Members of the Association are invited to attend and participate in the business meeting.

Election of officers, under the provisions of the new Constitution and By-Laws, will take place at this time.

Convocation Ceremony

The Convocation Ceremony, at which certificates of affiliation will be presented in person to newly elected Members, Associate Fellows, Fellows and those advanced in the various categories during the year, will follow the Annual Meeting of the Association at 5:00 P.M., on Monday afternoon, 17 September 1951, at The Drake in Chicago, Ill.

This year again, those participating in the Convocation Ceremony will wear academic costume, and an interesting program has been planned.

Members, their families, guests and friends are invited to attend.

President's Annual Reception

The President's Annual Reception, again sponsored by Winthrop-Stearns, Inc., will be held immediately following the Convocation Ceremony on Monday evening, 17 September 1951, at 6:30 P.M. Members of the Association, their friends, guests, as well as those present with the technical exhibits are cordially invited to attend. Admission cards may be secured at the time of registration at the registration desk.

Scientific Exhibits

Following the successful scientific exhibit at the Fifteenth Annual Convention we are again having scientific exhibits as a part of the scientific program of the Sixteenth Annual Convention. A separate room has been set aside for these exhibits and a certificate will be awarded for the best exhibit presented.

Annual Banquet

The Annual Banquet of the National Gastroenterological Association will be held at The Drake in Chicago, Ill., on Tuesday evening, 18 September 1951, at 7:00 P.M. to be preceded by cocktails.

Course in Postgraduate Gastroenterology

Immediately following our Sixteenth Annual Convention, the National Gastroenterological Association is conducting a Course in Postgraduate Gastroenterology on 20, 21, 22 September 1951, at The Drake in Chicago, Ill.

A distinguished faculty chosen, from the medical schools in and around the Chicago area headed, by Dr. Owen H. Wangensteen, Professor and Chairman of Department of Surgery, University of Minnesota Medical School, Co-chairman and Surgical Co-ordinator, and Dr. I. Snapper, Director of Medical Education of The Mt. Sinai Hospital, New York City, Co-Chairman and Medical Co-ordinator will present the Course.

Admission to the Course will be limited to those who hold matriculation cards indicating that they have paid the $50.00 fee for the Course.

New Type Commercial Exhibit

Inaugurating a change in policy, the National Gastroenterological Association this year has limited its commercial and technical exhibits to those concerns, other than book dealers and instrument makers, who are able to present an exhibit of scientific interest rather than the showing of a few pharmaceutical preparations.

This marks a forward step in commercial exhibits, the results of which will serve as a basis for exhibits at other conventions.

Special Luncheon

A special luncheon for representatives of the pharmaceutical concerns exhibiting at our convention and members and guests of the Association attending the convention will be held at The Drake in Chicago, Ill., on Tuesday, 18 September 1951.

The purpose of this luncheon, (tickets for which may be obtained without charge at the registration desk on the convention floor) is to promote a closer understanding between the medical profession and representatives of the pharmaceutical concerns.

Nominating Committee Report

The nominating committee of the National Gastroenterological Association, consisting of Dr. William W. Lermann,. Pittsburgh, Pa., chairman; Dr. C. J. Tidmarsh, Montreal, Canada; Dr. G. Randolph Manning, New York, N. Y. and Dr. E. A. Marshall, Cleveland, Ohio met in New York City in July 1951 and submitted the following slate of candidates to be voted upon at the annual meeting of the National Gastroenterological Association in September.

President-Elect .....Felix Cunha, M.D., San Francisco, Calif.
1st Vice-President ... Sigurd W. Johnsen, M.D., Passaic, N. J.
2nd Vice-President ...Lynn A. Ferguson, M.D., Grand Rapids, Mich.
3rd Vice-President ... James T. Nix, M.D., New Orleans, La.
4th Vice-President ... Arthur A. Kirchner, M.D., Los Angeles, Calif.
Secretary-General ....Roy Upham, M.D., New York, N. Y.
Secretary .....A. X. Rossien, M. D., Kew Gardens, N. Y.
Treasurer .....Elihu Katz, M.D., New York, N. Y.

For Members of the National Council

For 4 years .....Ludwig Frank, M.D., Charleston, W. Va.
Lester R. Whitaker, M.D., Portsmouth, N. H.
Bruce C. Lockwood, M.D., Detroit, Mich.
Harry M. Eberhard, M.D., Philadelphia, Pa.
Joseph Shaiken, M.D., Milwaukee, Wisc.

For 2 years .....Yves Chaput, M.D., Montreal, Canada
I. R. Jankelson, M.D., Boston, Mass.

Additional nominations, signed by 15 Fellows in good standing, may be presented to the Secretary 30 days prior to the meeting.

Errata

In the discussion by Dr. Hyman I. Goldstein of the article "Surgery in Massive Hemorrhage" which appeared on page 445 of the June 1951 issue, in the 2nd paragraph from the bottom of the page, reference was made to "the late Donald C. Balfour, of the Mayo Clinic."

This was a typographical error and should have read "Donald C. Balfour, *late* of the Mayo Clinic."

In the article "Remarks about Ulcer and Ulceriform Cancer of the Stomach" by Dr. Rene A. Gutmann which appeared in the June 1951 issue, the line beginning "five or ten of them to say in bed." should have read "five or ten of them *yearly* to stay in bed."

On page 453 of the same article, in the next to the last line at the bottom of the page, the sentence "The lymphatics were involved." should read "The lymphatics were *not* involved."

Program

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

SIXTEENTH ANNUAL CONVENTION
17, 18, 19 SEPTEMBER 1951
and
COURSE IN POSTGRADUATE GASTROENTEROLOGY
20, 21, 22 SEPTEMBER 1951

THE DRAKE
Lake Shore Drive and Upper Michigan Avenue
Chicago, Ill.

Members of the medical profession are cordially invited to attend the convention sessions.

Attendance at the Postgraduate Course is limited to those who have paid the matriculation fee.

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REGISTRATION—All members and guests should register. Identification badges for admittance to meetings will be given to those who register. These should be worn at all times during the session. Registration will take place at the registration desk on the convention floor.

LADIES REGISTRATION—At the registration desk on the Convention Floor. Registration facilities will be open at 8:30 each morning. Information concerning the various activities and events will be available there.

MEETINGS are held on Daylight Saving Time and will begin promptly at the time specified.

COURSE IN POSTGRADUATE GASTROENTEROLOGY—Admittance only upon presentation of official matriculation card.

SCIENTIFIC EXHIBITS—Will be in the Exhibit Hall and will be open daily, Monday to Thursday.

TECHNICAL EXHIBITS under the direction of Mr. Steven K. Herlitz, Exhibit Manager, will be open Monday to Thursday.

Those attending the Convention are urged to take advantage of the time in between the presentation of papers and sessions, to visit the technical exhibits and become acquainted with the many new products and new equipment on display.

VISIT THE EXHIBITS

Program

SIXTEENTH ANNUAL CONVENTION
NATIONAL GASTROENTEROLOGICAL ASSOCIATION

SCIENTIFIC SESSIONS
17, 18, 19 SEPTEMBER 1951
and
COURSE IN POSTGRADUATE GASTROENTEROLOGY
20, 21, 22 SEPTEMBER 1951

THE DRAKE
Lake Shore Drive and Upper Michigan Avenue
Chicago, Ill.

SPEAKERS AND OFFICERS OF INSTRUCTION

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BARRY J. ANSON, M.A., Ph.D. (Med. Sc.), Professor of Anatomy, Northwestern University Medical School, Chicago, Ill.

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LEONIDAS H. BERRY, M.S., M.D., Professor of Gastroenterology and Gastroscopy, Cook County Graduate School of Medicine; Senior Attending Physician and Chairman, Department of Medicine, Provident Hospital, Chicago, Ill.

R. RUSSELL BEST, B.S., M.D., Professor of Surgery, University of Nebraska College of Medicine, Omaha, Neb.

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JOSEPH L. CARROLL, M.D., Resident in Gastroenterology, Jefferson Medical College and Hospital, Philadelphia, Pa.

DALE W. CREEK, A.B., M.D., Medical Staff of The Sansum Clinic, Santa Barbara Cottage Hospital, St. Francis Hospital and Santa Barbara General Hospital, Santa Barbara, Calif.

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EARL J. HALLIGAN, M.D., F.A.C.S., F.I.C.S., Chief Surgeon and Director of Department of Surgery, Jersey City Medical Center, Chief Surgeon, St. Francis Hospital, Jersey City, N. J., Consulting Surgeon, Margaret Hague Maternity and St. Mary's Hospitals, Jersey City, N. J.

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N. C. JEFFERSON, M.D., Provident Hospital and Michael Reese Hospital, Gastrointestinal Research Department, Chicago, Ill.

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OWEN H. WANGENSTEEN, B.A., M.D., Ph.D., Professor and Chairman, Department of Surgery, University of Minnesota Medical School, Minneapolis, Minn.

C. WILMER WIRTS, B.S., M.D., Associate in Medicine and Chief, Gastrointestinal Clinic, Jefferson Medical College and Hospital, Philadelphia, Pa.

SCIENTIFIC SESSIONS

FIRST SESSION

MONDAY MORNING, 17 SEPTEMBER 1951

C. J. TIDMARSH, M.D., President, National Gastroenterological Association, Presiding.

9:00 A.M.

1. "Amebic Dysentery".

Speaker

DR. HOWARD B. SHOOKHOFF, New York, N. Y. (By invitation).

9:20 A.M.

Discussion to be opened by:

DR. FRANK C. VAL DEZ, Chicago, Ill. (By invitation).

9:30 A.M.

2. "The Use of ACTH in the Treatment of Ulcerative Colitis".

Speakers

DR. C. WILMER WIRTS and DR. JOSEPH L. CARROLL, Philadelphia, Pa. (By invitation).

9:50 A.M.

Discussion to be opened by:

DR. JOSEPH B. KIRSNER, Chicago, Ill. (By invitation).

10:00 A.M. Recess to visit the Commercial and Technical Exhibits.

10:15 A.M.

3. "Association of Tuberculosis with Gastroenteritis".

Speaker

DR. A. XERXES ROSSIEN, Kew Gardens, N. Y.

10:35 A.M.

Discussion to be opened by:

DR. ELIHU KATZ, New York, N. Y.

10:45 A.M.

4. "The Role of the Phrenic Nerve in Vagotomy and in Gastrointestinal Mechanisms".

Speakers

DR. H. NECHELES and DR. N. C. JEFFERSON, Chicago, Ill.

11:05 A.M.

General Discussion.

VISIT THE EXHIBITS

11:15 A.M.

5. "Cancer Chemotherapy".

Speaker

Dr. C. P. Rhoads, New York, N. Y. (By invitation).

11:35 A.M.

General Discussion.

SECOND SESSION

MONDAY AFTERNOON, 17 SEPTEMBER 1951

Harry M. Eberhard, M.D., Vice-President, National Gastroenterological Association, Presiding.

2:00 P.M.

SYMPOSIUM ON PEPTIC ULCER:

6. "The Physiological Aspects of Peptic Ulcer".

Speaker

Dr. A. C. Ivy, Chicago, Ill. (By invitation).

2:20 P.M.

7. "The Medical Aspects of Peptic Ulcer".

Speaker

Dr. David J. Sandweiss, Detroit, Mich.

2:40 P.M. Recess to visit the Commercial and Technical Exhibits.

3:10 P.M.

8. "The Surgical Aspects of Peptic Ulcer".

Speaker

Dr. Lester R. Dragstedt, Chicago, Ill. (By invitation).

3:30 P.M.

Discussion to be opened by:

Dr. Warren H. Cole, Chicago, Ill. (By invitation).

4:00 P.M.

ANNUAL MEETING OF THE ASSOCIATION—GENERAL ASSEMBLY.

5:00 P.M.

CONVOCATION: Presentation of Certificates.
See Special Program.

6:30 P.M.

PRESIDENT'S ANNUAL RECEPTION (Admission by card only, obtained at the time of registration).

THIRD SESSION

TUESDAY MORNING, 18 SEPTEMBER 1951

ROY UPHAM, M.D., Secretary-General, National Gastroenterological Association, Presiding.

9:00 A.M.

9. "Comparative Value of X-ray and Gastroscopy in 2,500 Gastroscopic Examinations".

Speaker

DR. LEONIDAS H. BERRY, Chicago, Ill.

9:20 A.M.

Discussion to be opened by:

DR. WILLIAM C. JACOBSON, New York, N. Y.

9:30 A.M.

10. "Single and Multiple Polyps of the Colon and Rectum—Management".

Speaker

DR. R. RUSSELL BEST, Omaha, Neb. (By invitation).

9:50 A.M.

Discussion to be opened by:

DR. MORRIS L. PARKER, Chicago, Ill. (By invitation).

10:00 A.M. Recess to visit the Commercial and Technical Exhibits.

10:30 A.M.

SYMPOSIUM ON THE PANCREAS:

11. "The Pathological Aspects of Pancreatic Disease".

Speaker

DR. HANS POPPER, Chicago, Ill. (By invitation).

10:50 A.M.

12. "The Medical Aspects of Pancreatic Disease".

Speaker

DR. EARL E. GAMBILL, Rochester, Minn. (By invitation).

11:10 A.M.

13. "The Surgical Aspects of Pancreatic Disease".

Speaker

DR. CHARLES B. RIPSTEIN, Brooklyn, N. Y.

11:30 A.M.

Discussion to be opened by:

DR. M. I. GROSSMAN, Chicago, Ill. (By invitation).

VISIT THE EXHIBITS

FOURTH SESSION

TUESDAY AFTERNOON, 18 SEPTEMBER 1951

FELIX CUNHA, Vice-President, National Gastroenterological Association, Presiding.

2:00 P.M.

14. "Gastric Secretion in Normal Individuals and Patients with Peptic Ulcer".

Speaker

DR. ERWIN LEVIN, Chicago, Ill. (By invitation).

2:20 P.M.

Discussion to be opened by:

DR. ROWLAND W. RICKETTS, Merchantville, N. J.

2:30 P.M.

15. "The Pathophysiology of Gallbladder Disease".

Speaker

DR. BRUCE C. LOCKWOOD, Detroit, Mich.

2:50 P.M.

Discussion to be opened by:

DR. SAMUEL WEISS, New York, N. Y.

3:00 P.M. Recess to visit the Commercial and Technical Exhibits.

3:30 P.M.

16. "Liver Disease and Liver Lymph".

Speaker

DR. JAMES T. NIX, New Orleans, La.

3:50 P.M.

Discussion to be opened by:

DR. EMANUEL RAPPAPORT, Jamaica, N. Y.

4:00 P.M.

17. "Gynecic Endocrine Factors in Relation to Alimentary Tract Function and Abdominal Symptomatology".

Speaker

DR. A. E. RAKOFF, Philadelphia, Pa. (By invitation).

4:20 P.M.

General Discussion.

7:00 P.M.

ANNUAL BANQUET—THE DRAKE, Chicago, Ill.

VISIT THE EXHIBITS

FIFTH SESSION

WEDNESDAY MORNING, 19 SEPTEMBER 1951

SIGURD W. JOHNSEN, M.D., Secretary, National Gastroenterological Association, Presiding.

9:00 A.M.

18. "Treatment of Intestinal Infections Due to Low-grade Pathogens".

Speakers

DR. ALBERT MILZER and HELEN MAC LEAN, Chicago, Ill. (By invitation).

9:20 A.M.

Discussion to be opened by:

DR. WILLIAM W. LERMANN, Pittsburgh, Pa.

9:30 A.M.

19. "The Consideration of the Nutrition of Visceroptotic Patients".

Speaker

DR. GARFIELD G. DUNCAN, Philadelphia, Pa. (By invitation).

9:50 A.M.

Discussion to be opened by:

DR. ROY UPHAM, New York, N. Y.

10:00 A.M. Recess to visit the Commercial and Technical Exhibits.

10:30 A.M.

SYMPOSIUM ON PSYCHOSOMATIC MEDICINE:

20. "The Role of the Psychiatrist in Handling Psychosomatic Problems".

Speaker

DR. HERMAN M. SEROTA, Chicago, Ill. (By invitation).

10:50 A.M.

21. "The Role of the Internist in Handling Psychosomatic Problems".

Speaker

DR. SIDNEY A. PORTIS, Chicago, Ill. (By invitation).

11:10 A.M.

Discussion to be opened by:

DR. FRANZ ALEXANDER, Chicago, Ill. (By invitation).

11:20 A.M.

22. "Esophagitis, 'Spontaneous' Perforation of the Esophagus and Cardiospasm".

Speaker

DR. OWEN H. WANGENSTEEN, Minneapolis, Minn.

11:50 A.M.

General Discussion.

VISIT THE EXHIBITS

SIXTH SESSION

WEDNESDAY AFTERNOON, 19 SEPTEMBER 1951

WILLIAM W. LERMANN, President, National Gastroenterological Association, Presiding.

2:00 P.M.

SYMPOSIUM ON CARCINOMA:

23. "The Early Diagnosis of Cancer of the Digestive Tract".

Speakers

DR. WALTER L. PALMER and DR. JOSEPH B. KIRSNER, Chicago, Ill. (By invitation).

2:20 P.M.

24. "The Indications for Conservative Rectal Resection".

Speaker

DR. GEORGE T. PACK, New York, N. Y. (By invitation).

2:40 P.M. Recess to visit the Commercial and Technical Exhibits.

3:10 P.M.

25. "Radiology in Cancer of the Digestive Tract".

Speaker

DR. FRED J. HODGES, Ann Arbor, Mich. (By invitation).

3:30 P.M.

Discussion to be opened by:

DR. DANELY P. SLAUGHTER, Chicago, Ill. (By invitation).

SEVENTH SESSION

WEDNESDAY EVENING, 19 SEPTEMBER 1951

ANTHONY BASSLER, M.D., Honorary President, National Gastroenterological Association, Presiding.

8:00 P.M.

26. "The Influences of Dietary and Living Habits on Certain Metabolic Processes".

Speaker

DR. DALE W. CREEK, Santa Barbara, Calif.

8:10 P.M.

27. "Radiologic Management of Carcinoma of the Esophagus".

Speakers

DR. HENRI LE CLAIRE and E. M. JAPHA, Cincinnati, Ohio.

VISIT THE EXHIBITS

8:20 P.M.

28. "The Management of Gastrointestinal Hemorrhage".

Speakers

Dr. N. E. Rossett and Dr. Samuel L. Stephenson, Memphis, Tenn.

8:30 P.M.

29. "Evaluation of the Ether Method for Dissolving Common Duct Stones Postoperatively".

Speaker

Dr. B. O. C. Pribram, New York, N. Y.

8:40 P.M.

30. "Significance of Markedly Enlarged Spleen in Cirrhosis of the Liver".

Speakers

Dr. Frederick Steigmann and Dr. E. Stevens, Chicago, Ill.

8:50 P.M. Recess to visit the Commercial and Technical Exhibits.

9:20 P.M.

31. "Clinical Evaluation of the Einhorn String Test".

Speakers

Dr. Henry A. Rafsky; Dr. Walter Lowenberg and Dr. Leroy Peterson, New York, N. Y.

9:30 P.M.

32. "Cholangitis".

Speakers

Dr. John M. McGowan and Dr. S. Albert Sarkisian, Boston, Mass.

9:40 P.M.

33. "The Lack of Correlation of Symptoms and Findings in Intestinal Obstruction".

Speakers

Dr. Helmuth Nathan and Dr. John Mosley, New York, N. Y.

9:50 P.M.

34. "An Overlooked Cause for Mortality in Acute Appendicitis".

Speaker

Dr. Edward F. Sciorsci, Hoboken, N. J.

10:00 P.M.

35. "The Sigmoidorectal Intussusception: A Common Clinical Syndrome".

Speaker

Dr. Emil Granet, New York, N. Y.

VISIT THE EXHIBITS

COURSE IN POSTGRADUATE GASTROENTEROLOGY

SURGICAL COORDINATOR AND CO-CHAIRMAN
OWEN H. WANGENSTEEN, B.A., M.D., Ph.D., Minneapolis, Minn.

MEDICAL COORDINATOR AND CO-CHAIRMAN
I. SNAPPER, M.D., Ph.D., New York, N. Y.

FIRST SESSION

THURSDAY MORNING, 20 SEPTEMBER 1951

9:00 A.M.
Address of Welcome—
WILLIAM W. LERMANN, M.D., President, National Gastroenterological Association.

9:15 A.M.
1. "The Oral Cavity in Health and Disease".

Speaker
DR. BERNARD SARNAT, Chicago, Ill.

9:45 A.M.
2. "The Anatomy of the Alimentary Tract".

Speaker
DR. BARRY J. ANSON, Chicago, Ill.

10:15 A.M. Recess to visit the Commercial and Technical Exhibits.

10:45 A.M.
3. "Histochemical Studies on the Gastrointestinal Tract".

Speaker
DR. GEORGE GOMORI, Chicago, Ill.

11:15 A.M.
4. "Diseases of the Esophagus".

Speaker
DR. SAUL MACKLER, Chicago, Ill.

SECOND SESSION

THURSDAY AFTERNOON, 20 SEPTEMBER 1951

2:00 P.M.
5. "Problems of Refractory Peptic Ulcer Cases".

Speaker
DR. JOSEPH B. KIRSNER, Chicago, Ill.

VISIT THE EXHIBITS

2:30 P.M.

6. "The Possible Role of Vagotomy Combined with Gastroenterostomy as a Method of Surgical Treatment for the Patient with Chronic Duodenal Ulcer".

Speaker

Dr. Edwin M. Miller, Chicago, Ill.

3:00 P.M. Recess to visit the Commercial and Technical Exhibits.

3:30 P.M.

7. "Hepatic Lymphangitis".

Speaker

Dr. B. O. C. Pribram, New York, N. Y.

4:00 P.M.

8. "Reliability of Roentgenographic Diagnosis in Gastrointestinal Disease".

Speaker

Dr. Joseph Shaiken, Milwaukee, Wis.

THIRD SESSION

FRIDAY MORNING, 21 SEPTEMBER 1951

9:00 A.M.

9. "Gastroscopy".

Speaker

Dr. Leonidas H. Berry, Chicago, Ill.

9:30 A.M.

10. "Malignancy of the Duodenum".

Speaker

Dr. Earl J. Halligan, Jersey City, N. J.

10:00 A.M. Recess.

10:15 A.M.

11. "The Importance of Lymph Nodes in Gastrointestinal Carcinoma".

Speaker

Dr. R. K. Gilchrist, Chicago, Ill.

VISIT THE EXHIBITS

10:45 A.M.

12. "The Problem of Gastrointestinal Disturbances Attributed to Allergy".

Speaker

DR. THEODORE L. SQUIER, Milwaukee, Wis.

11:15 A.M.

13. "Subject to be Announced".

Speaker

DR. I. SNAPPER, New York, N. Y.

FOURTH SESSION

FRIDAY AFTERNOON, 21 SEPTEMBER 1951

2:00 P.M.

14. "Diseases of the Anus and Rectum".

Speaker

DR. CLEMENT L. MARTIN, Chicago, Ill.

2:30 P.M.

15. "Diagnosis and Management of Patients Bleeding from the Inferior Intestinal Tract".

Speaker

DR. J. GARROT ALLEN, Chicago, Ill.

3:00 P.M. Recess.

3:15 P.M.

16. "Intestinal Strangulation Obstruction".

Speaker

DR. HAROLD LAUFMAN, Chicago, Ill.

3:45 P.M.

17. "Gastrointestinal Obstruction in the Newborn due to Neuromuscular Imbalance".

Speaker

DR. WILLIS J. POTTS, Chicago, Ill.

6:30 P.M. Reception and Banquet—The Drake.

VISIT THE EXHIBITS

FIFTH SESSION

SATURDAY MORNING, 22 SEPTEMBER 1951

9:00 A.M.

18. "Anemias Resulting from Disturbances of Gastrointestinal Function".

Speaker

Dr. Frank H. Bethell, Ann Arbor, Mich.

9:30 A.M.

19. "Physiologic Basis for the Therapeutic Effects of Cortisone".

Speaker

Dr. Samuel Soskin, Chicago, Ill.

10:00 A.M. Recess.

10:15 A.M.

20. "The Treatment of Hepatic Cirrhosis and Its Complications".

Speaker

Dr. Mitchell Spellberg, Chicago, Ill.

10:45 A.M.

21. "Differential Diagnosis of Jaundice by Laboratory Test".

Speaker

Dr. Hans Popper, Chicago, Ill.

11:15 A.M.

22. "The Medical Aspects of Psychosomatic Medicine—A Practical Approach".

Speaker

Dr. Sidney A. Portis, Chicago, Ill.

11:45 A.M.

23. "Subject to be Announced".

Speaker

Dr. Owen H. Wangensteen, Minneapolis, Minn.

VISIT THE EXHIBITS

SCIENTIFIC EXHIBITS

The Scientific Exhibits will be in the Exhibit Hall and will be open at the following times:

MONDAY, 17 September 1951—12:00 Noon to 4:00 P.M.

TUESDAY, 18 September 1951—9:00 A.M. to 5:30 P.M.

WEDNESDAY, 19 September 1951—9:00 A.M. to 5:30 P.M.; 8:00 P.M. to 11:00 P.M.

THURSDAY, 20 September 1951—9:00 A.M. to 3:30 P.M.

BOOTH A **"An Evaluation of the Treatment of Colonic Stasis". Stasis".**
DR. HARRY BAROWSKY, New York, N. Y.

BOOTH B **"Tubeless Gastric Analysis with Indicator Exchange Compounds".**
DRS. HARRY L. SEGAL, LEON L. MILLER and JOHN J. NORTON, Rochester, N. Y.

BOOTH C **"Colectomy with Primary Anastomosis".**
DRS. S. L. GOVERNALE and CARLO FIORETTI, Chicago, Ill.

BOOTH D **"What is Adequate Medical Therapy in Peptic Ulcer".**
DR. EDWARD A. MARSHALL, Cleveland, Ohio

BOOTH E **"A Symbol Observed on Migraine Cases".**
DR. THEODORE S. HEINEKEN, Bloomfiield, N. J.

BOOTH F **"The Antithrombin Test for Acute Pancreatitis".**
DRS. IRVING INNERFIELD and ALFRED ANGRIST, Nyack, N. Y.

TECHNICAL EXHIBITORS

(Those attending the Convention sessions are urged to take advantage of the time in between the presentation of papers and sessions, to visit the technical exhibits and become acquainted with many new products and new equipment on display)

THE BILHUBER-KNOLL CORP., Orange, New Jersey (Booth 6), will again present their medicinal chemicals and products, such as the antispasmodic, *Octin;* the sedo-spasmolytic, *Valoctin;* the nonbarbiturate sedative, *Bromural;* the potent analgesic, *Dilaudid;* the nonirritant intestinal astringent, *Tannalbin,* etc. Your inspection and discussion of these time-tested prescription medicinals will be welcome.

BURTON, PARSONS & CO., Washington, D. C. (Booth 16), will exhibit for the first time at any meeting *Konsyl* and *L. A. Formula,* the two original products made from Plantago Ovata Coating and widely used in cases where such bulk-producing agents are indicated. A new and improved version of the *L. A. Formula* will be shown.

VISIT THE EXHIBITS

CAMERON SURGICAL SPECIALTY COMPANY, Chicago Ill. (Booth 1), will display the new flexible esophagoscope known as the *Boroscope* and designed by Dr. Edwin Boros of New York. It is Cameron built, of stainless steel, black lines. No rubber "finger" at the end to obscure vision. It is passed under direct vision. The *Omniangle Gastroscope* is generally accepted throughout the world as the standard. No other gastroscope oven approaches the efficiency of the *Cameron Omniangle Gastroscope*. Other items are the *Crump Ductlite* and *Esophageal Stylet* and the large assortment of stainless steel and Surgimold distally and proximally lighted rectal endosopes.

THE COCA-COLA COMPANY, Atlanta, Georgia (Lounge), will serve ice-cold Coca-Cola through the courtesy and cooperation of the Coca-Cola Company.

EDER INSTRUMENT COMPANY, Chicago, Ill. (Booth 13) will exhibit a complete line of Gastroscopic Instruments, the standard flexible and also the adjustable tip Gastroscope. The Flexible Esophagoscope with optical examining telescope which includes a special biopsy cutter should be of interest to the profession. Their latest development a proctoscopic table converted into a standard examining table, rectal instruments and a moist heat pad will be shown at their booth.

GRUNE & STRATTON, INC., New York, New York (Booth 2), will display the following important books devoted to gastroenterology and allied fields: *Bauer: Differential Diagnosis of Internal Diseases; Crohn: Regional Ileitis; Schindler: Gastritis; Nissen: Duodenal and Jejunal Peptic Ulcer; Allen: The Kidney, Medical and Surgical Diseases; Narath: Renal Pelvis and Ureter; Storch: Fundamentals of Clinical Fluoroscopy*. These and many other books will be of definite interest to the gastroenterologist.

IVES-CAMERON COMPANY, INC. of New York (Booth 7). The theme of their exhibit will be "The Use Of Surface Active Agents in Medicine." Bibliographies compiled by the I.V.C. Research Department on the use of *Monooleate* will be available. Company representatives will gladly discuss the application of this surface action agent as it concerns I.V.C. products *Monitan* and *Oxsorbil*.

J. B. LIPPINCOTT COMPANY, Philadelphia, Pa. (Booth 21), presents, for your approval, a display of professional books and journals geared to the latest and most important trends in current medicine and surgery. These publications, written and edited by men active in clinical fields and teaching, are a continuation of more than 100 years of traditionally significant publishing.

MALLON CHEMICAL CORP., New York, New York (Booth 14), subsidiaries of the DOHO CHEMICAL CORPORATION makers of *Auralgan, O-Tos-Mo-San* and *Rhinalgan* are pleased to exhibit *Rectalgan*, the liquid topical anesthesia for the immediate symptomatic relief of pain and discomfiture in hemorrhoids, pruritus and perineal pain following suturing, also many other uses pre- and postoperatively.

THE WM. S. MERRELL COMPANY, Cincinnati, Ohio (Booth 3), will present *Bentyl* Hydrochloride for prompt, effective and *comfortable* relaxation of gastrointestinal smooth muscle spasm. *Bentyl* is a high milligram potency nonnarcotic antispasmodic with two-fold musculotropic and neurotropic action. Effective therapeutically without atropine-like side actions in functional gastrointestinal disorders. *Bentyl* is particularly suited for prolonged administration without habituation or increased tolerance.

THE NATIONAL DRUG COMPANY, Philadelphia, Pa. (Booth 24), pioneer in the clinical application of resin therapy will feature *Natrinil*, a cation exchange resin for the control of edema; *Resinat*, a polyamine exchange resin for the treatment of peptic ulcer, and *Resion*, an intestinal absorbent. Trained represntatives will be in attendance to discuss our resin preparations and other specialties.

A. H. ROBINS COMPANY, INC., Richmond, Va. (Booth 17), will feature at their display the sedative-antispasmodic, *Donnatal;* the antirheumatic, *Pabalate: Entozyme*, digestant with the unique "peptomatic" action; the highly effective antitussive-expectorant, *Robitussin; Allbee with C,* high potency B-complex capsule with ascorbic acid; and *Phenaphen with Codeine,* our new analgesic. Robins' Medical Service Representatives will welcome the privilege of discussing with physicians attending the Assembly these and other products in the company's line of prescription specialties.

WILLIAM H. RORER, INC., Philadelphia, Pa. (Booth 18), will display *Suspension Maalox*, a new antacid suspension composed of special colloidal grades of Magnesium Hydroxide and Aluminum Hydroxide. *Maalox* was originated to provide the patient with all the advantages of Aluminum Hydroxide Gel USP but to eliminate the constipation often caused by the drug, and to improve its taste. It has been subjected to intense clinical testing and found advantageous, particularly for peptic and gastric ulcer and for heartburn due to gastritis.

RYSTAN COMPANY, INC., Mount Vernon, New York (Booth 20), will exhibit new Chloresium Tablets, the water-soluble chlorophyll deodorant report in the August 1951 REVIEW OF GASTROENTEROLOGY as effectively controlling colostomy odors. Also exhibited will be Chloresium Powder for peptic ulcers, which combines the tissue-repairing properties of water-soluble chlorophyll with proven antacids in highly mucilaginous okra base.

SANDOZ PHARMACEUTICALS, New York, N. Y. (Booth 15), invite you with a great deal of pleasure to visit their scientific exhibit on Vascular Headaches. Their representatives will gladly welcome you.

SCHENLEY LABORATORIES, INC., Lawrenceburg, Ind. (Booth 5). For useful information on their progressive line, visit their exhibit. *Titralac*, Schenley's unique antacid is now available in liquid as well as in tablet and powder form. *Sedamyl* is also featured. Providing sedation without hypnosis, *Sedamyl* is ideal for daytime use to relieve anxiety states common to today's harried life.

G. D. SEARLE & CO., Chicago, Ill. (Booth 12). You are cordially invited to visit their booth where their representatives will be happy to answer any questions regarding Searle Products of Research. Featured will be *Banthine*, the true anticholingeric drug for the treatment of peptic ulcers; *Dramamine*, for the prevention and active treatment of motion sickness; and *Alidase*, Searle brand of hyaluronidase which permits subcutaneous feedings at intravenous speed. Other time proven products of Searle Research on which information may be obtained are Searle *Aminophyllin* in all dosage forms, *Metamucil*, *Ketochol*, *Floraquin*, *Kiophyllin*, *Diodoquin*, *Pavatrine*, and *Pavatrine* and *Phenobarbital*.

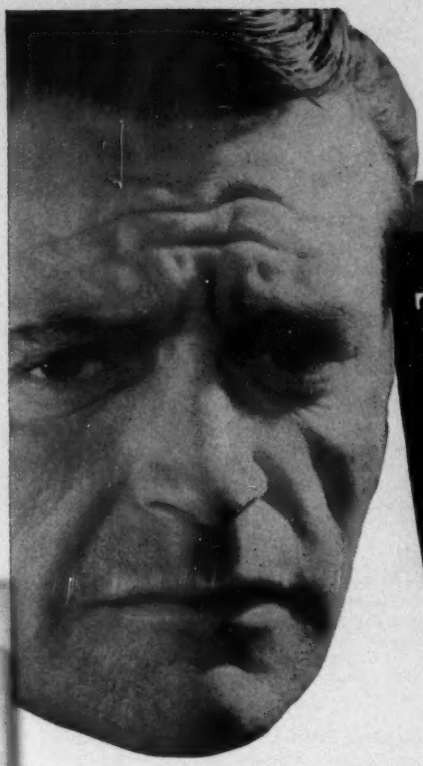
SENTRAL LABORATORIES, INC., Cedar Rapids, Iowa (Booth 10), will display; 1. An enzyme tablet composed of the major enzymes of the gastrointestinal tract, protected from the acid media for those enzymes operating in the duodenal and small intestines, which we have had considerable research done upon, and which was found to be of value in excess cholesterol conditions, whether the patient was an atheriosclerotic or a diabetic; 2. A liquid amino acid from an acid digest of protein. Will have plenty of factual information here on this product, with serum protein fractionations to prove its efficacy; 3. A tablet supplying all the mineral needs of the body, with report on same from Hollywood Presbyterian Hospital.

E. R. SQUIBB & SONS, Long Island City, N. Y. (Booth 4). In support of the active program which has been arranged, you will find the Squibb representative glad to discuss all related products. Also, for your convenience, selected professional literature will be available which you may take or request us to send to your home. Please visit the Squibb booth.

FREDERICK TROUT COMPANY, Atlanta, Ga. (Booth 19), will feature *Combichole*, a combination of chemically pure bile acids. A hydrocholeratic *plus* fat emulsifier in a single tablet. Also; *Calsamate*, a quick acting analgesic buffered with calcium glutamate to prevent side reactions.

WYETH, INCORPORATED, Philadelphia, Pa. (Booth 22). Their representative will be on hand to welcome you to their exhibit, and to supply you with information and samples of many outstanding new and established ethical pharmaceutical preparations. Regardless of your specialty you will undoubtedly find many therapeutic agents suited to your particular practice from among the preparations listed in the Wyeth catalogue.

WINTHROP-STEARNS INC., New York, N. Y. (Booth 8) extends a cordial invitation to visit its booth, where representatives will be on hand to serve you. Featured will be *Creamalin*, nonalkaline, nonabsorbable antacid; *Mucilose Compound Tablets*, the new physiologic bulk laxative; *Diodrast* 35%, for operative and postoperative cholangiography; *Essenamine Compound*, pleasant tasting protein concentrate.



The seemingly intractable ulcer patient

His pain is severe
His recurrences are frequent
He bleeds repeatedly
He is easily constipated

This "hard-to-keep-well" ulcer patient need not be a cause for undue concern until Tricreamalate has been given adequate trial. When other medications fail, Tricreamalate, a combination of specially prepared gastric antacids with distinct advantages will often

stop pain more quickly
prevent recurrences
control bleeding
without side effects

Tricreamalate is a highly reactive amorphous acid soluble aluminum hydroxide *plus* hydrated magnesium trisilicate. Tablets: 2 to 4, after each feeding. Liquid: 2 to 4 teaspoonfuls after each feeding.

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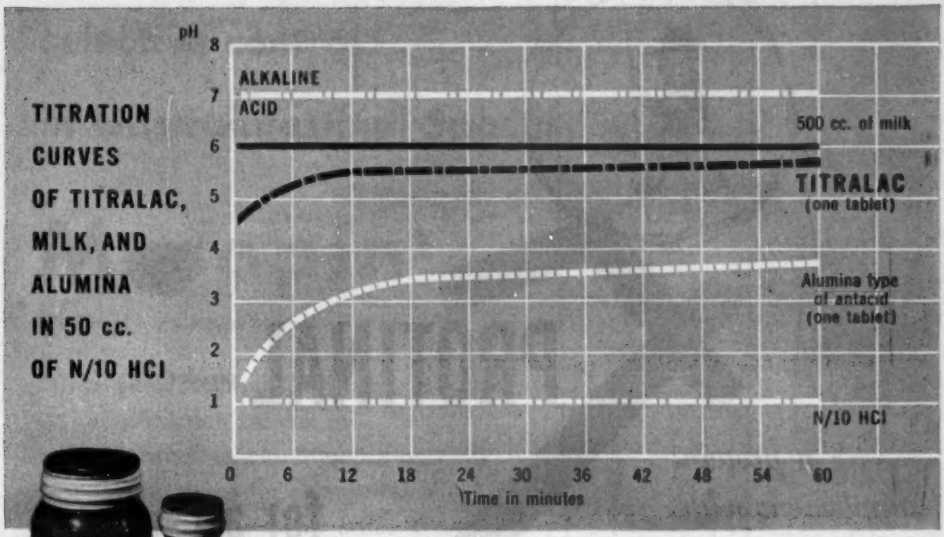

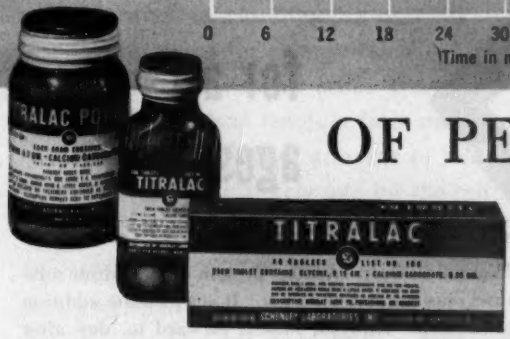

OF PEPTIC ULCER

Gastroenterologists have long endorsed the use of milk, when practicable, for its ideal acid-converting power and buffering capacity.[1, 2] In a recent comprehensive paper, Aaron[3] and others[4, 5, 6] express a preference for calcium carbonate as the antacid to be employed.

TITRALAC, by combining proper proportions of purified calcium carbonate and the amino acid glycine, *provides an acid-converting and buffering effect practically equivalent to that of fresh milk*, as shown in the above chart.* Just 1 TITRALAC tablet is equivalent to an 8-ounce glass of milk in antacid effect and provides quick and long-lasting relief from the distressing symptoms of hyperacidity.

The very agreeable taste of soft-massed TITRALAC tablets, which is achieved without employing taste-disguising, acid-generating sugars in the formula, makes them as acceptable to patients as a mint after dinner. Prescribing TITRALAC eliminates the probability of unfavorable reactions often associated with the taking of metallic-tasting, astringent tablets or liquids, and ensures adherence to the prescribed dosage.

TITRALAC tablets are supplied in bottles of 100 and convenient-to-carry packages of 40. TITRALAC powder is also available, in 4-oz. jars.

REFERENCES

1. Rossett, N. E., and Flexner, J.: Ann. Int. Med. 18: 193 (1944). 2. Freezer, C. R. E.; Gibson, C. S., and Matthews, E.: Guy's Hosp. Reports 78: 191 (1928). 3. Aaron, A. H.; Lipp, W. F., and Milch, E.: J. A. M. A. 139: 514 (Feb. 19) 1949. 4. Kirsner, J. B., and Palmer, W. L.: Illinois M. J. 94: 357 (Dec.) 1948. 5. Kimball, S.: in Practice of Medicine (Tice). Hagerstown, Md., W. F. Prior Company, Inc., 1948; p. 210. 6. Special Article: M. Times 76: 10 (Jan.) 1948.

*The formula of TITRALAC is one whose composition and mode of action are recognized by U.S. Patent No. 2,429,596.

Samples and literature to physicians upon request.

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for all ages!

Protinal Powder, an intact protein-carbohydrate mixture, does not cloy the palate. It is a pleasant addition to the diet—enjoyed, looked forward to, day after day, week after week.

Easy to mix...Protinal Powder is micro-pulverized and mixes far more readily with water, milk, and other foods than do ordinary granule preparations.

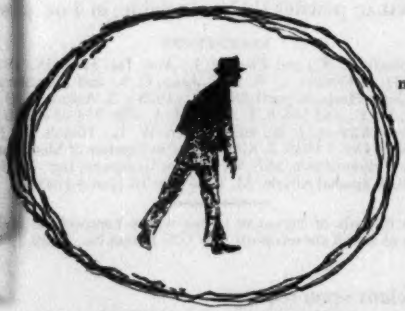
Virtually sodium and fat free... contains less than 0.03% sodium and less than 1% fat.

Each 30 Gm. (2 tablespoonfuls) contains:

Protein (N x 6.25, casein)	18.4 Gm. (61.25%)
Carbohydrate...vanillin flavored . .	9.0 Gm. (30%)
...chocolate flavored . .	7.2 Gm. (24%)

micro-pulverized

Vanillin or chocolate flavored in 8-ounce, 1-lb. and 5-lb. bottles. Literature and samples on request.



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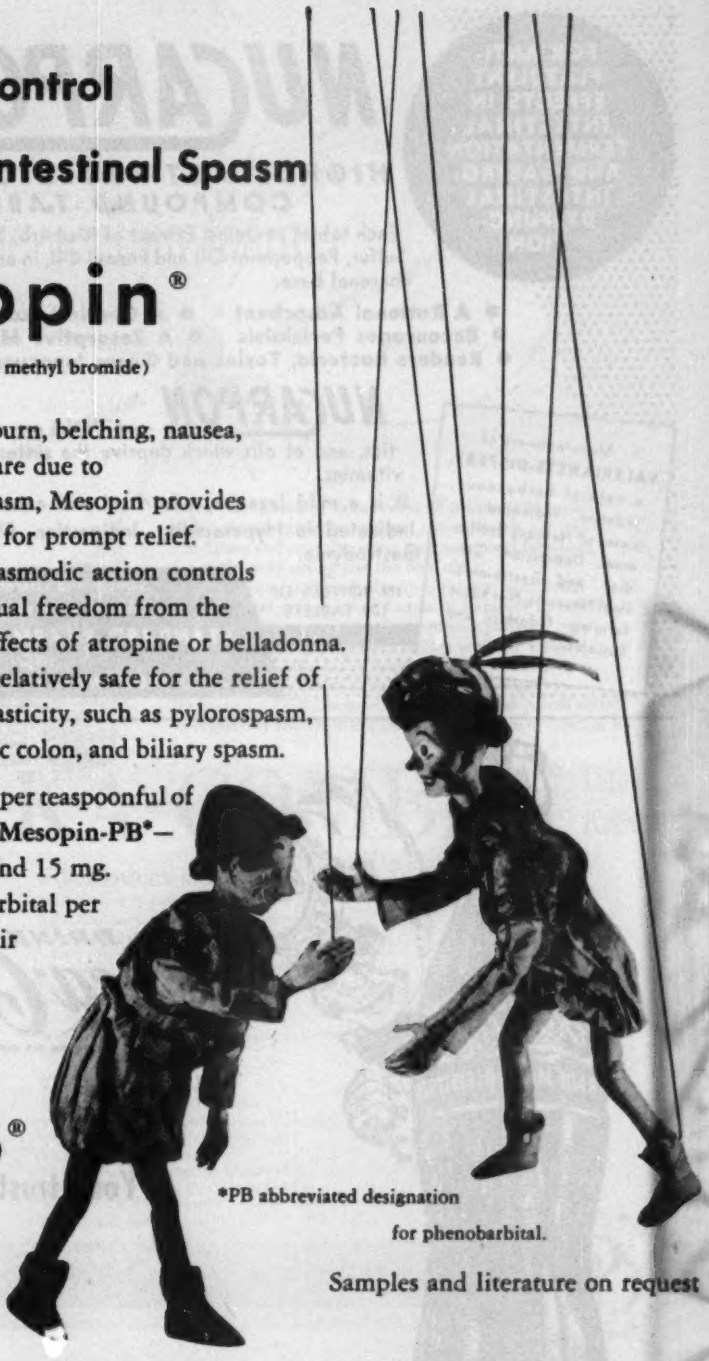
of Gastrointestinal Spasm

Mesopin®

(brand of homatropine methyl bromide)

When pain, heartburn, belching, nausea, or unstable colon are due to gastrointestinal spasm, Mesopin provides an effective means for prompt relief. Its selective antispasmodic action controls spasticity with virtual freedom from the undesirable side effects of atropine or belladonna. Thus, Mesopin is relatively safe for the relief of gastrointestinal spasticity, such as pylorospasm, cardiospasm, spastic colon, and biliary spasm.

Mesopin—2.5 mg. per teaspoonful of elixir or per tablet. **Mesopin-PB***—2.5 mg. Mesopin and 15 mg. (1/4 gr.) phenobarbital per teaspoonful of elixir or per tablet.



Endo®

*PB abbreviated designation for phenobarbital.

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Endo Products, Inc., Richmond Hill 18, N. Y.

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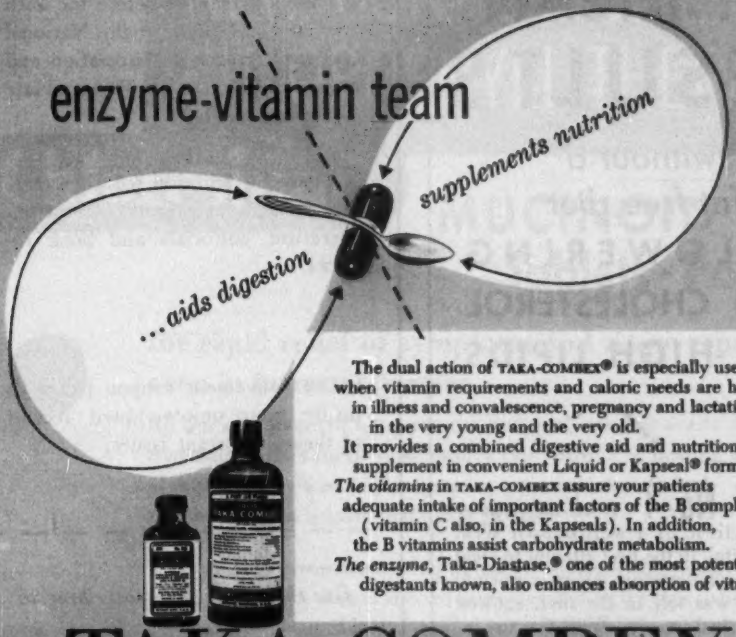
enzyme-vitamin team



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The vitamins in TAKA-COMBEX assure your patients adequate intake of important factors of the B complex (vitamin C also, in the Kapseals). In addition, the B vitamins assist carbohydrate metabolism.

The enzyme, Taka-Diastase,® one of the most potent starch digestants known, also enhances absorption of vitamin B.

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TAKA-COMBEX Kapseals

Each Kapseal contains:

Taka-Diastase (*Aspergillus oryzae* enzymes)	2½ gr.
Vitamin B_1 (Thiamine Hydrochloride)	10 mg.
Vitamin B_2 (Riboflavin)	10 mg.
Vitamin B_6 (Pyridoxine Hydrochloride)	0.5 mg.
Pantothenic Acid (Sodium Salt)	3 mg.
Nicotinamide (Niacinamide)	10 mg.
Vitamin C (Ascorbic Acid)	30 mg.

With other components of the Vitamin B Complex derived from liver.
In bottles of 100 and 1000.

TAKA-COMBEX Liquid

Each teaspoonful (4 cc.) contains:

Taka-Diastase (*Aspergillus oryzae* enzymes)	2½ gr.
Vitamin B_1 (Thiamine Hydrochloride)	2 mg.
Vitamin B_2 (Riboflavin)	1 mg.
Vitamin B_6 (Pyridoxine Hydrochloride)	0.5 mg.
Pantothenic Acid (As the Sodium Salt)	2 mg.
Nicotinamide (Niacinamide)	5 mg.

In 16 ounce bottles.

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Chloresium MUCINOID Tablets • Powder

for rapid relief of symptoms and tissue repair even in intractable cases

All the advantages of CHLORESIUM POWDER* are now available in convenient *tablet* form: same unique combination of healing agent plus antacids in a mucin-like base — same superior clinical results — and in a form that's easy to take.

highly concentrated, purified water-soluble chlorophyll promotes healing of affected areas, duplicating the outstanding results obtained in treatment of external lesions.

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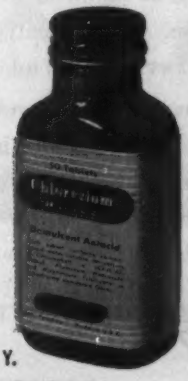
prompt, sustained antacid action — without undesirable side effects — provided by magnesium trisilicate and aluminum hydroxide.

packaging: CHLORESIUM MUCINOID is available in bottles of 50 and 200 tablets and in boxes of 25 powders.*



*CHLORESIUM POWDER will continue to be available in boxes of 25 envelopes but will now be sold under the name CHLORESIUM MUCINOID.

RYSTAN COMPANY, INC. Mount Vernon, N. Y.

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FAST RELIEF

in gastric hyperacidity

When patients with functional gastro-intestinal disorders complain of epigastric distress, heartburn, bloating or dyspepsia, Creamalin gives relief *in minutes.* Creamalin is amorphous acid soluble aluminum hydroxide, the form with fast neutralizing action.

FAST HEALING

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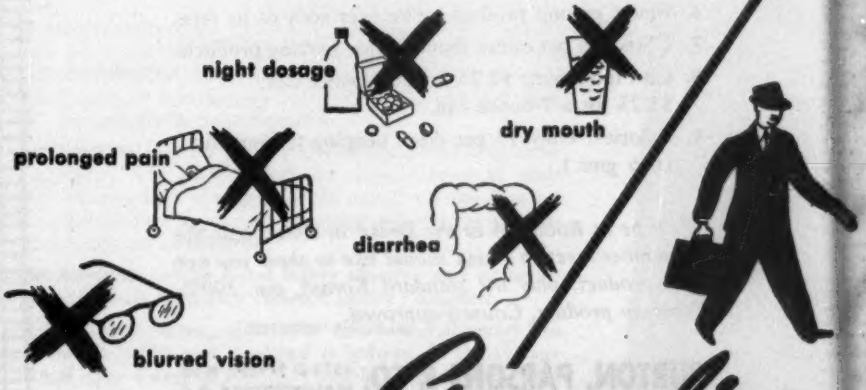
Creamalin heals peptic ulcer as quickly as 7 to 10 days. A reactive, demulcent type of gel, it buffers acidity for prolonged periods. Around the clock control of gastric secretion is usually maintained by taking Creamalin *during the day only.*[1]
Because Creamalin is unabsorbed, it is safe for prolonged use and does not impose biochemical complications.[2] Creamalin spares the peptic ulcer patient



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AMORPHOUS ACID SOLUBLE REACTIVE ALUMINUM HYDROXIDE

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1. Breuhaus, H. C., Akre, C. H., and Eyerly, J. B.: *Gastroenterology,* 16:172, Sept., 1950.
2. Jordan, Sara M.: *Ann. West. Med. & Surg.,* 4:133, Mar., 1950.

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All physicians are invited

to a launching . . .

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Low Toxicity

Practically devoid of by-effects in therapeutic dosage

RELIEVES spastic pain and discomfort

a more effective antispasmodic (anticholinergic) drug

Bronchospasm, cardiospasm, pylorospasm, biliary spasm, intestinal spasm, ureteral spasm and other spastic disorders of the gastro-intestinal and genito-urinary tracts are quickly and effectively combated with **NEOTROPINE* Hydrochloride** 'Warner,' the latest development of Warner research laboratories. This new anticholinergic drug "blocks" the undesirable nerve impulses.

NEOTROPINE* Hydrochloride is of low toxicity and its use attended by minimum by-effects. The usual unwelcome complications of antispasmodic therapy such as dryness of the mouth and disturbances of the cardiovascular, respiratory or visual systems are not encountered in the use of **NEOTROPINE***.

NEOTROPINE* Hydrochloride will be found highly effective as a parasympathetic inhibitor in all spastic (smooth muscle) disorders.

Dosage: One tablet, 50 mg., of **NEOTROPINE* Hydrochloride** orally every 4 to 6 hours, usually before each meal and at bedtime. In the average case a total daily dosage of 200 mg. (4 tablets) provides an adequate and satisfactory antispasmodic action.

Packaging: **NEOTROPINE* Hydrochloride** 'Warner' is available in the form of sugar-coated oral tablets, 50 mg. each, bottles of 100.

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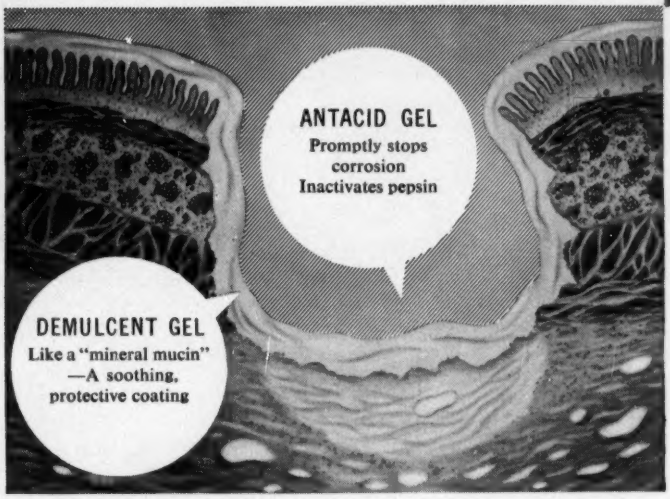

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Relieves pain in minutes

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